

Improving the End-of-Life Experience in Singapore: Building Capacity in Palliative Care Education and Research

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Singapore is ageing rapidly. Whereas ageing symbolises advancements that the country has made in public health and medicine over the past few decades, it has brought new concerns regarding care for the elderly, and especially in the last years or months of life. A report commissioned by the Lien foundation in 2010 ranked Singapore 18th out of 40 countries included on a “quality of death index” that compared standards of end-of-life (EOL) care across countries.¹ This, in turn, motivated the formulation of the National Strategy for Palliative Care in Singapore. The report recognised palliative care services to be an essential part of the healthcare system that should be provided to all patients with life limiting illnesses. The report also recommended adequate education and training of health care professionals and investments in research to improve quality of palliative care and to inform policy making.²

Although advancements have been made, as with many countries, Singapore still comes up short in the delivery of palliative care services. Many patients at the EOL die in pain³ and not at the place of their choice (which tends to be at home),⁴ and after a carousel of visits to the emergency department and other healthcare providers. There are simply not enough clinicians and other healthcare staff trained in providing palliative care to meet the increasing demand for EOL services. In fact, an Educational Needs Assessment conducted by the Lien Centre for Palliative Care (LCPC) showed that non-palliative care clinicians do not have the confidence or skills required to deliver basic palliative care services. This is partly because palliative care is either under-represented or non-existent in undergraduate and postgraduate curriculums of medical, nursing and allied health disciplines. This needs to change as both general practitioners and specialists will see a larger proportion of patients at the EOL in the coming decades. While education and training activities, such as the Singapore Hospice Council Post Graduate Doctors’ course in Palliative Medicine and specialist and advanced diplomas in Palliative Care Nursing, have equipped some doctors and nurses with

palliative care skills and knowledge, these opportunities need to be expanded to include other cadres of healthcare professionals such as social workers and pharmacists. The latter groups, in particular, have clear lack of training opportunities in this field. In addition, having clinical guidelines to ensure consistent standards of care across institutions and individual practices will also improve the quality of EOL care being provided. At present, Singapore has no national clinical practice guidelines for palliative care, though talks are underway with the Ministry of Health to address this gap.

EOL care can also be improved through high quality research efforts. This research needs to be methodologically rigorous, outcomes based and with clear implications for patient care and policy making. For instance, there is a lack of comprehensive data regarding cost and utilisation of services across the various entities that provide care to dying patients. World Innovation Summit for Health (WISH) EOL Report 2013,⁵ authored by luminaries in health policy and palliative care, highlighted the importance of quantifying the cost of dying and determining ways to lower costs while improving quality of care. Availability of such data in Singapore could be useful for identifying inappropriate use of services, quality improvement initiatives, resource allocation and budgeting, and for policy analysis, including analyses of upcoming changes to Medishield, which are expected to increase coverage (and likely expenditures) for EOL services. More formative research is also needed in several areas, including pain management, understanding patient preferences, improving financing models, and in health and risk communication, among others.

Patient care can be seriously compromised if interventions are accepted into routine practice without high quality evidence of effectiveness in the local context; the type of evidence that typically only comes via randomised controlled trials (RCTs), which are the gold standard in building an evidence base. Take, for example, the Liverpool EOL care pathway. This pathway was widely implemented

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in the UK and in other countries in Europe. Unfortunately, it was implemented on a wide scale without the benefit of a trial and was later shown to be widely misused, which resulted in poor outcomes that led to it quickly being phased out.⁶ A rigorous evaluation through a RCT could have identified the shortcomings and avoided this failure. More recently, a high quality RCT showed that a common communication skills-building workshop did not improve the quality of communication but instead increased depressive symptoms among patients.⁷ Even Advanced Care Planning, something that is widely recommended to be integrated into standard practice in Singapore, needs further study given the limited evidence for its effectiveness locally and internationally.⁸

There are many barriers to expanding education and research in palliative care. Yet, the benefits to patient care for our most vulnerable patients require us to work to overcome these barriers. There is hope for the future. Efforts are being made to expand palliative care education and training activities to allied healthcare workers. LCPC has also established a research incubator that provides funding and research support for investigator-initiated research in palliative care.⁹ Through greater education and training to increase service capacity, and high quality research, we can work to improve the EOL experience for all Singaporeans.

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Determinants of Health-Related Quality of Life Among Community Dwelling Elderly

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Abstract

Introduction: This study determines the associations between self-reported chronic conditions, limitations in activities of daily living and health-related quality of life (HRQoL) among community dwelling elderly in Singapore. **Materials and Methods:** A population-based cross-sectional survey was conducted among a random sample of 4200 residents from 58 blocks of dwellings in Marine Parade housing estate between April and May 2011. A structured questionnaire was used to collect data on demographic characteristics; chronic disease profile, health screenings, healthcare utilisation, physical activity, activities of daily living (ADL) and functional ability and health related quality of life. Quality of life was assessed using European Quality of life 5 Domain (EQ-5D). Ordinary least squares (OLS) regression was used to identify independent predictors of health related quality of life. **Results:** A total of 2454 respondents for included for analysis. Most of the respondents were females (57.2%) and aged between 65 and 74 years (48.5%). Among them, 79.1% of the respondents were Chinese. Approximately three-fourth (77.5%) of the survey respondents reported having at least one of the 13 chronic medical conditions; high blood pressure (57.7%), high blood cholesterol (51.6%), diabetes (22.9%) were the most commonly reported conditions. Independent predictors of HRQoL with greatest decrements in EQ-5D index and visual analog scores (VAS) were unemployment, self-reported depression, arthritis and osteoporosis and ADL limitations for activities such as “unable to shower”, “unable to do housework” and elderly with depressive symptoms (GDS score ≥ 5). **Conclusion:** The study had identified predictors of HRQoL in elderly Singapore residents and also provides community-based EQ-5D index and VAS scores associated with a wide variety of chronic conditions and ADL limitations.

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Key words: Activities of daily living, Chronic conditions, EQ-5D, Health-related quality of life, elderly, Predictive factors, Singapore, Utility values

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Introduction

Singapore is experiencing an unprecedented age shift as the post-war baby boomers turn 65 years in 2012. Currently there are 378,700 people aged 65 and above, and these numbers are estimated to go up to 600,000 by 2020.¹ These growing elderly population have multiple coexisting medical conditions which are often associated with functional decline, disability, higher hospital admissions² and emergency department attendances.³ Health is the most important determinant of the elderly person's quality of life. It affects all other areas of their life, including their willingness to seek and accept help.⁴ Hence, addressing elderly's healthcare needs is vital to improve their health-related quality of life (HRQoL).⁵

Clinicians, researchers, and policy makers are increasingly

recognising the importance of measuring HRQoL in informing patient management, policy decisions⁶ and resource allocation.⁷ Health utilities (HU) are commonly used for assessing HRQoL in evaluation of healthcare interventions such as the cost-utility analyses (CUA).^{8,9} In CUA, a utility score is assigned to the health state on the cardinal scale in which dead = 0 and perfect health = 1 which indicates respondent's preferences for different outcomes. This utility score is incorporated into quality-adjusted life-year (QALYs) which combines life expectancy and quality of life (HU) into a single index. The European quality of life scale (EQ-5D) is the frequently used HU instrument for calculating QALYs based on actual measurements of patients HRQoL.¹⁰

The EQ-5D instrument consists of a 5-item descriptive

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system of health states and a visual analog scale (VAS). Scores for the 5 health states can be converted into a utility index score by using scores from value sets (preference weights) elicited from a general population. The best-known preference weights were derived from samples of the United Kingdom (UK).¹¹ These preference weights are applied to other populations when country-specific weights are not available with certain limitations.¹²⁻¹⁵ Unfortunately, preference weights of EQ-5D for Singapore is not yet available, so applying other existing preference weight from UK was essential to obtain EQ-5D index values for Singapore. In this study, we report associations between self-reported chronic conditions, limitations in activities of daily living and health-related quality of life (HRQoL) in a community living elderly population in Singapore.

Materials and Methods

Study Design

The data used in this paper were derived from a larger cross-sectional survey carried out to assess health status, health and social care resource needs and utilisation profile of individuals aged 60 years and above in the Marine Parade housing estate of Singapore. The study sample size was calculated to estimate the proportion of functional disability in the community. Using an estimated proportion of 2% of older people who need support for at least one activity of daily living, an estimation error of 0.5%, and non-response rate of 40%, a sample size of 4200 older people were required.

A random sample of 4200 elderly residents from 58 housing development blocks (HDBs) in Marine Parade housing estate between April and May 2011 were surveyed. A team of trained interviewers administered the survey through face-to-face interviews with residents in their homes. Singapore Citizens or Permanent Residents aged 60 years and above living in 2- to 5-room housing in Marine Parade were included in the survey. The survey questionnaire elicited information on respondent's demographic characteristics; physical health (chronic disease profile, health screenings, healthcare utilisation, physical activity, 12-item activities of daily living (ADL),¹⁶ Instrumental Activities of Daily Living (IADL)¹⁷ and health related quality of life (Questionnaire - Appendix). Locally validated 15-item Geriatric Depression Scale (GDS-15)¹⁸ and the Abbreviated Mental Test (AMT)¹⁹ were used as screening tools for depressive symptoms and cognitive impairment. Health related quality of life was measured using EQ-5D. Validated Mandarin and Malay versions of EQ-5D was used for Chinese and Malay respondents respectively.²⁰⁻²² The questions in the survey were subjected to cognitive testing, and were translated and back-translated from English to Mandarin and Malay. Residents residing

in institutions or who were out of the country during the period of data collection were excluded. Similarly, residents who refused to participate, and who were not contactable after 3 household visits were considered non-responders.

Statistical Analysis

All data are presented as means (SD) or as proportions (weighted). All estimates were weighted; sampling weights were incorporated into the analyses to adjust for planned oversampling of selected age groups to reflect the general Marine Parade population. Responses to the EQ-5D items were transformed into an EQ-5D index score using UK preference weights. Direct valuation of the respondent's current state of health was obtained from EQ-5D VAS. Associations between HRQoL and its potential determinants were examined by univariate analysis and then by ordinary least squares (OLS) regression model using the STATA SVY REGRESS procedure. This procedure enabled us to incorporate the sampling weights in the model. Nine socio-demographic co-variables (i.e. gender, ethnicity, education, work status, income, ownership status, housing status, self-reported chronic conditions and activities of daily living) were included in the model as categorical variables, except the continuous variable for age, GDS-15 and AMT scores. All 13 chronic conditions were defined by dummy variables and served as independent predictors in the models. For parsimony, no interaction terms were included in the models. All the responses coded as refused, unknown, or missing were treated as missing data. All analyses were conducted with the Stata Statistical Software, version 12.0 (Stata Corp., College Station, Texas). The findings were considered statistically significant at the 5% level ($P < 0.05$). Approval for this study was obtained from the Institutional Review Board of the National Healthcare Group, Singapore.

Results

A total of 3752 residents were eligible for inclusion in the study of which 2558 residents were interviewed, giving an overall response rate of 68.2%. Of these, only 2454 respondents were included in the analysis, after excluding 104 proxy responses. The socio-demographic characteristics of the survey respondents and estimates of EQ-5D index and VAS are summarised in Table 1. After applying sampling weights, the mean age of the sample was 69.2 years (SD = 6.9), with a maximum of 99 years. Mean EQ-5D index and VAS were 0.94 (SD 0.14) and 79.17 (SD 13.71) respectively. Of the sample, 48.5% were 65 to 74 years of age, 57.2% were females, 79.1% were Chinese, 36% had secondary education, 80% were flat owners, 34% lived in a 3 room HDB, 40% were retirees and 25.8% had an average monthly income of \$500 to <\$1000 SGD.

Table 1. Socio-demographic Characteristics and Estimates of EQ-5D Index and VAS

Variables	Categories	n = 2454 (%)*	EQ-5D index	EQ-5D VAS
			Mean $\pm$ SD	Mean $\pm$ SD
Age group (years)	60 – 64	810 (33.0)	0.95 $\pm$ 0.12	80.26 $\pm$ 13.04
	65 – 74	1189 (48.5)	0.94 $\pm$ 0.14	79.11 $\pm$ 13.90
	75 – 84	342 (13.9)	0.91 $\pm$ 0.15	78.57 $\pm$ 13.39
	85 and above	113 (4.6)	0.86 $\pm$ 0.17	73.65 $\pm$ 15.90
Gender	Male	1050 (42.8)	0.95 $\pm$ 0.13	79.17 $\pm$ 13.82
	Female	1404 (57.2)	0.93 $\pm$ 0.14	79.16 $\pm$ 13.63
Ethnic group	Chinese	1940 (79.1)	0.94 $\pm$ 0.13	79.15 $\pm$ 13.48
	Indian	114 (4.6)	0.88 $\pm$ 0.23	80.23 $\pm$ 15.47
	Malay	301 (12.3)	0.92 $\pm$ 0.16	78.22 $\pm$ 14.74
	Others	99 (4.0)	0.94 $\pm$ 0.10	81.13 $\pm$ 12.61
Education	Degree and Higher	96 (3.9)	0.94 $\pm$ 0.15	80.65 $\pm$ 10.75
	Diploma	148 (6.0)	0.95 $\pm$ 0.09	79.38 $\pm$ 12.01
	Junior College	168 (6.8)	0.96 $\pm$ 0.08	79.64 $\pm$ 12.07
	Secondary	887 (36.1)	0.95 $\pm$ 0.11	80.07 $\pm$ 13.20
	Primary	600 (24.4)	0.94 $\pm$ 0.14	78.99 $\pm$ 13.74
	No formal qualification	555 (22.6)	0.90 $\pm$ 0.18	77.45 $\pm$ 15.58
Ownership‡	Owner	1954 (79.6)	0.94 $\pm$ 0.12	79.39 $\pm$ 13.25
	Tenant	386 (15.7)	0.90 $\pm$ 0.19	78.75 $\pm$ 15.73
Housing type	1 and 2 rooms	394 (16.1)	0.90 $\pm$ 0.19	78.98 $\pm$ 15.82
	3 rooms	832 (33.9)	0.94 $\pm$ 0.13	78.72 $\pm$ 13.63
	4 rooms	613 (25.0)	0.94 $\pm$ 0.13	80.29 $\pm$ 13.18
	5 rooms	615 (25.1)	0.95 $\pm$ 0.11	78.76 $\pm$ 12.82
Work status	Full time	389 (15.9)	0.96 $\pm$ 0.09	81.13 $\pm$ 12.85
	Housewife	714 (29.1)	0.93 $\pm$ 0.14	78.52 $\pm$ 14.08
	Part-time	304 (12.4)	0.96 $\pm$ 0.10	81.63 $\pm$ 13.07
	Retiree	992 (40.4)	0.93 $\pm$ 0.15	78.52 $\pm$ 13.19
	Unemployed	55 (2.2)	0.80 $\pm$ 0.28	71.51 $\pm$ 21.12
Average monthly income†	<\$500	627 (25.6)	0.91 $\pm$ 0.17	76.94 $\pm$ 15.58
	\$500 to <\$1000	633 (25.8)	0.94 $\pm$ 0.12	79.92 $\pm$ 13.35
	\$1000 to <\$2000	373 (15.2)	0.95 $\pm$ 0.10	80.06 $\pm$ 12.44
	\$2000 to <\$3000	112 (4.6)	0.97 $\pm$ 0.08	79.38 $\pm$ 11.07
	\$3000 and above	96 (3.9)	0.97 $\pm$ 0.07	82.17 $\pm$ 10.69

SD: Standard deviation

*The percentages are adjusted by the population sampling weights from Marine Parade.

†Ownership – others (n = 114) not shown in the Table.

‡Income not available for 613 respondents.

Prevalence of Self-reported Chronic Conditions

About three-fourth (77.3%) of the sample reported having at least one chronic medical condition and 4.8% reported more than 5 chronic conditions (Table 2). After adjusting for over-sampling, the percentage of respondents reporting each condition are shown in Table 2. Among the chronic conditions reported by respondents, high blood pressure (57.7%), high blood cholesterol (51.7%), diabetes (22.9%), arthritis (16.6%), were the most commonly reported,

followed by falls (13.9%), hearing problems (13.3%) and urinary incontinence (12.7%). There was a significant decrease in EQ-5D index and VAS scores with increasing chronic conditions. (Trend test for ordered groups, $P = 0.0001$) (Table 3).

Socio-demographics, Self-reported Chronic Conditions, Limitations in ADL and HRQoL

There was a significant positive correlation between ED-

Table 2. Health Status, Activities of Daily Living and Estimates of EQ-5D Index and VAS

Variables	Categories	n = 2454 (%)*	EQ-5D index	EQ-5D VAS
			Mean $\pm$ SD	Mean $\pm$ SD
Self-reported chronic conditions†	Diabetes	560 (22.9)	0.97 $\pm$ 0.09	77.15 $\pm$ 14.82
	High blood pressure	1404 (57.7)	0.97 $\pm$ 0.08	77.75 $\pm$ 13.57
	High cholesterol	1267 (51.7)	0.97 $\pm$ 0.09	77.83 $\pm$ 13.86
	Heart attack	117 (4.9)	0.86 $\pm$ 0.21	74.19 $\pm$ 16.55
	Heart failure	60 (2.5)	0.88 $\pm$ 0.21	73.43 $\pm$ 15.81
	Chest pain	93 (3.9)	0.82 $\pm$ 0.27	72.32 $\pm$ 17.82
	Stroke	83 (3.5)	0.79 $\pm$ 0.25	70.30 $\pm$ 16.96
	Kidney disorders	61 (2.5)	0.81 $\pm$ 0.28	70.13 $\pm$ 16.47
	Asthma	102 (4.2)	0.94 $\pm$ 0.18	75.82 $\pm$ 13.97
	Dementia	7 (0.3)	0.90 $\pm$ 0.13	78.14 $\pm$ 19.97
	Depression	35 (1.4)	0.86 $\pm$ 0.11	67.97 $\pm$ 18.26
	Arthritis	406 (16.6)	0.94 $\pm$ 0.10	75.58 $\pm$ 14.92
	Osteoporosis	230 (9.6)	0.90 $\pm$ 0.16	74.45 $\pm$ 15.87
	History of falls	332 (13.9)	0.89 $\pm$ 0.19	75.50 $\pm$ 16.33
	Urinary Incontinence	309 (12.7)	0.92 $\pm$ 0.16	74.96 $\pm$ 15.20
	Hearing problem	314 (13.3)	0.93 $\pm$ 0.13	79.76 $\pm$ 13.36
Activities of daily living (ADL)	Unable to feed	9 (0.4)	0.43 $\pm$ 0.34	58.63 $\pm$ 21.33
	Unable to dress	31 (1.3)	0.52 $\pm$ 0.34	62.13 $\pm$ 15.52
	Unable to get out of bed / chair	46 (1.9)	0.59 $\pm$ 0.31	65.40 $\pm$ 18.37
	Unable to shower	47 (1.9)	0.59 $\pm$ 0.32	62.76 $\pm$ 14.97
	Unable to use the toilet	34 (1.4)	0.53 $\pm$ 0.31	61.88 $\pm$ 15.54
	Unable to use the telephone	40 (1.6)	0.66 $\pm$ 0.31	68.62 $\pm$ 17.56
	Unable to get to places within walking distance	177 (7.2)	0.73 $\pm$ 0.27	68.24 $\pm$ 16.54
	Unable to shop for groceries / clothes	180 (7.3)	0.74 $\pm$ 0.26	68.32 $\pm$ 16.10
	Unable to prepare meals	142 (5.8)	0.71 $\pm$ 0.29	68.08 $\pm$ 16.76
	Unable to do housework	230 (9.4)	0.77 $\pm$ 0.26	69.28 $\pm$ 15.67
	Unable to take his/her medicines	74 (3.0)	0.69 $\pm$ 0.31	66.77 $\pm$ 16.87
	Unable to handle his/her money	57 (2.3)	0.68 $\pm$ 0.31	69.24 $\pm$ 21.32
Geriatric depression scale (GDS-15)‡	Respondents with depressive symptoms (GDS-15 score $\geq$ 5)	188 (7.7)	0.75 $\pm$ 0.26	66.10 $\pm$ 15.33
	Respondents without depression symptoms (GDS-15 score $\leq$ 4)	2241 (91.3)	0.95 $\pm$ 0.11	80.28 $\pm$ 12.95
Cognitive impairment§	AMT score $\leq$ 7	168 (6.8)	0.82 $\pm$ 0.24	71.47 $\pm$ 14.27
	AMT score $\geq$ 8	2281 (92.9)	0.95 $\pm$ 0.12	79.76 $\pm$ 13.46

SD: Standard deviation

*The percentages are adjusted by the population sampling weights from Marine Parade.

†Only one chronic condition reported by 5 or more people is included in the Table.

AMT score§ and GDS-15‡ score are not available for 5 and 25 respondents respectively, hence their number would not add up to the total, n.

Table 3. Self-reported Chronic Conditions and EQ-5D Index and VAS Scores (n = 2454)

No of chronic diseases	Frequency n, %	Weighted, %	Cumulative, %	ED-5D index	EQ-5D VAS
				Mean $\pm$ SD	Mean $\pm$ SD
0	564 (23.0)	22.7	23.0	0.97 $\pm$ 0.08	83.29 $\pm$ 12.36
1	543 (22.1)	22.1	45.1	0.96 $\pm$ 0.10	80.03 $\pm$ 12.61
2	615 (25.1)	25.2	70.2	0.94 $\pm$ 0.12	78.87 $\pm$ 13.21
3	445 (18.1)	18.1	88.3	0.91 $\pm$ 0.15	77.16 $\pm$ 13.92
4	171 (7.0)	7.1	95.3	0.85 $\pm$ 0.22	73.98 $\pm$ 16.01
5	78 (3.2)	3.2	98.5	0.87 $\pm$ 0.18	73.22 $\pm$ 13.67
6	8 (0.3)	1.2	99.6	0.76 $\pm$ 0.26	72.30 $\pm$ 18.53
7	14 (0.5)	0.3	99.9	0.63 $\pm$ 0.40	63.13 $\pm$ 25.77
≥ 8	3 (0.1)	0.1	100.0	0.64 $\pm$ 0.11	55.00 $\pm$ 7.07

Table 4. Regression Coefficients for Significant Predictors of the EQ-5D VAS and Index Score

Categories	EQ-5D VAS ($R^2 = 0.12$)		EQ-5D index ($R^2 = 0.36$)	
	UnS (b)	S(B)	UnS (b)	S(B)
Intercept	87.587†		0.976†	
Age	0.076	0.038	0.001†	0.053
Females	− 1.453*	− 0.052*	0.001	0.004
Indian	3.140*	0.048	− 0.042†	− 0.064
Work status : Unemployed	− 6.510†‡	− 0.070	− 0.098†‡	− 0.105
Income <\$500	− 3.845*	− 0.122	− 0.023	− 0.073
Owner	0.395	0.012	− 0.032†	− 0.094
Tenant	− 2.963	− 0.079	− 0.063†‡	− 0.167
Housing : 4 rooms	− 5.610*‡	− 0.194	− 0.021	− 0.070
Housing: 1 – 2 rooms	− 6.217†‡	− 0.197	− 0.023	− 0.072
Self-reported Chronic Conditions				
Urinary incontinence	− 2.7892†	− 0.0654	− 0.0127	− 0.0304
Hearing problems	− 2.1323†	− 0.0523	− 0.0069	− 0.0173
Falls	− 1.7425	− 0.0431	− 0.0180*	− 0.0453
High blood pressure	− 1.7948†	− 0.0644	− 0.0112	− 0.0407
Chest pain	− 1.7148	− 0.0250	− 0.0493†	− 0.0733
Dementia	8.8467	0.0333	0.1452†	0.0557
Depression	− 6.6825*‡	− 0.0514	− 0.1425†‡	− 0.1116
Arthritis	− 3.1215†	− 0.0822	− 0.0436†	− 0.1169
Osteoporosis	− 2.7822*	− 0.0580	− 0.0511†	− 0.1085
Activities of Daily Living				
Unable to feed	− 8.1468	− 0.0307	− 0.1799†‡	− 0.0690
Unable to dress	− 7.6619	− 0.0575	− 0.1916†‡	− 0.1464
Unable to get out of bed/chair	11.8686†	0.1140	0.0124	0.0121
Unable to shower	− 9.2657*	− 0.0903	− 0.0637	− 0.0632
Unable to use the toilet	− 0.4442	− 0.0037	− 0.0944†	− 0.0806
Unable to use the telephone	9.1073†	0.0748	0.0208	0.0174
Unable to shop for groceries / clothes	− 0.4929	− 0.0092	− 0.0412*	− 0.0781
Unable to do housework	− 4.8532†‡	− 0.1023	0.0054	0.0117
Unable to handle his/her money	− 3.0912	− 0.0310	− 0.0647†	− 0.0660
Geriatric Depression Scale (GDS-15) score	− 0.1195†	− 0.0870	− 0.0007†	− 0.0552

* $P < 0.05$, † $P < 0.01$

UnS:Unstandardised coefficients; S:Standardised coefficients

‡Top 5 predictors associated with lower absolute EQ-5D index / VAS with largest coefficients

Reference category: Males, Chinese, Degree, working-full time, income SGD \$3000 and above, ownership status others, housing status (5-room hdb), absence of the above stated chronic conditions and no limitations in the above ADLs.

5D index scores and the VAS score (Spearman correlation coefficient, $r = 0.28$, $P = 0.0001$). ED-5D index and VAS scores decreased significantly with increasing age, lower housing type, income and education. (Trend test for ordered groups, $P = 0.0001$). Females, respondents with lower educational qualification, tenants and unemployed respondents had lower EQ-5D and VAS scores. (KW test, $P < 0.001$). (Table 1) Similarly respondents with depression and limitations in activities of daily living such as “feeding” had the lowest EQ-5D index and VAS scores compared to others. Respondents with cognitive impairment (AMT score ≤ 7) and those with depressive symptoms (GDS-15 score ≥ 15) had a significantly lower EQ-5D index and VAS scores. (KW test, $P < 0.001$) (Table 2).

Predictors of the EQ-5D VAS and Index Score

We explored associations between chronic conditions, limitations in activities of daily living and HRQoL after statistically controlling for age, gender, ethnicity, education, work status, income, ownership status and housing status. The regression coefficients of EQ-5D and VAS models are presented in Table 4. The amount of variance explained by EQ-5D VAS and index were 13% and 36% respectively. Table 4 also presents the standardised regression coefficients which help us examine the magnitude of the association between independent variables and the dependent variable; the larger the coefficient, the greater the association.

The top 5 independent predictors associated with a lower absolute EQ-5D index were unemployment, house ownership, self-reported depression, limitations in activities of daily living such as feeding and dressing. Similarly, the top 5 independent predictors associated with larger coefficients for EQ-5D VAS were unemployment, respondents living in 4-room and 2-room HDB (Housing and Development Board) flat, self-reported depression and limitations in activities of daily living such as housework. Respondents who were unemployed, with income less than \$500, with depression, arthritis, osteoporosis and higher GDS-15 scores were associated with substantially lower absolute EQ-5D index and VAS scores. Respondents with depression, arthritis and osteoporosis had more than a 2.5-point decrease in the EQ-5D index and more than a 0.4-point decrease in the EQ-5D VAS score. Females, unemployed, income $< \$500$, elderly staying in 1 to 2 room and 4-room HDB flats, respondents with urinary incontinence, hearing problems, high blood pressure, depression, arthritis, elderly with limitations in activities of daily living such as “showering”, “feeding” and “dressing” and “unable to do housework” and higher GDS-15 score had a significant negative association with EQ-5D VAS scores (Table 4). Increasing age, being unemployed, income $< \$500$, owners, tenants, respondents with chest pain, dementia, depression,

arthritis, osteoarthritis, respondents who were unable to feed, dress, use the toilet, to shop for groceries, handle money and respondents with higher GDS-15 scores had significant negative association with EQ-5D index scores (Table 4).

Discussion

This is the first study to report HRQoL and its association between self-reported chronic conditions and limitations in activities of daily living among the community dwelling elderly in Singapore. In our study, about 3 out of 4 (77%) elderly respondents had at least one chronic condition. High blood pressure, high blood cholesterol, diabetes, arthritis were the most commonly reported conditions. The self-reported prevalence of high blood pressure, arthritis, falls and urinary incontinence were lower while the high blood cholesterol, diabetes and hearing problems were marginally higher than previous reports from a National Health Surveillance Survey.²³ Our study sample was not nationally representative. In addition, self-reported health underestimates true disease prevalence in older populations.^{24,25} Hence, the observed self-reported estimates of chronic conditions were lower than national estimates.

HRQoL decreased with age and number of chronic diseases. It was also lower for females than males. Elderly without employment, with no education and lower income ($< \$500$ per month) had the lowest scores, similar to studies elsewhere.²⁶⁻²⁸ Elderly with self-reported depression and limitations in activities of daily living such as feeding, toileting and dressing had the lowest HRQoL. Similarly, HRQoL was significantly lower for elderly with depressive symptoms (GDS-15 score ≥ 5) and those with cognitive impairment (AMT score ≤ 7). In our study, Indians had poor HRQoL when compared to the other ethnic groups. Chan et al,²⁹ reported gender and ethnic differences in self-reported health, older women and Indians had poorer health. In a study done by Wee HL³⁰ on HRQoL among patients with diabetes mellitus using SF-6D, Indians with DM were found to have lower HRQoL than the other ethnic groups. Findings from our study and literature confirm that ethnic difference does exist in HRQoL. Independent predictors of HRQoL with greatest decrements in EQ-5D index and VAS scores were unemployment, self-reported depression, arthritis and osteoporosis and ADL limitations for activities such as “unable to shower”, “unable to do housework” and elderly with depressive symptoms (GDS score ≥ 5). Similar results were observed elsewhere.³¹⁻³⁴

HRQoL measured by EQ-5D index score estimated using preference weights from UK population correlated well with VAS scores which were direct measurement of respondent’s self-rated health, similar findings were observed by Luo Nan et al.³⁵ In our study, the HRQoL model explained only

13% of the variance in EQ-5D VAS and explained 36% of the variance in the EQ-5D index using UK preference weights. In a recent study, Luo Nan et al found that Chinese and English speaking Singaporeans respond differently to the EQ-5D VAS. In our study we used Mandarin and Malay versions of EQ-5D for Chinese and Malays.³⁵ Among the ethnic groups, HRQoL model explained 13% and 19% of the variance in EQ-5D VAS in Chinese and Malays respectively. However, for Indians, 44% of the variation in EQ-5D VAS was explained by the model. Previous studies have shown that non-English versions of EQ-VAS (especially Chinese version) were not sensitive for self-assessment of health in the Singaporean population.³⁵ Hence, use of non-English version of EQ-5D VAS in this population needs further investigation.

The study had few methodological limitations. First, EQ-5D preference weights for Singapore are not available yet, hence we used the UK preference weights for estimating EQ-5D index values for Singapore. Second, chronic conditions were self-reported. As such it is unknown if the chronic conditions reported were actually diagnosed by a physician. Third, the causal relationship between self-reported chronic conditions, activities of daily living and HRQoL cannot be determined due to the cross-sectional nature of the data.

Limitations notwithstanding, this study provides crucial information on the predictors of HRQoL among community dwelling elderly in Singapore. This information would aid planning active aging interventions to improve the health related quality of life of the country's rapidly aging population. Cost-effectiveness analyses of treatment options are often underpinned by decision analytic models. These models typically assess the benefits of treatment options in terms of the QALY gain associated with avoiding a clinical event or alleviating a particular health condition. Consequently, in addition to the utility values associated with the event or health condition, analysts also need the utility values associated with not experiencing the event or the health condition, i.e. the baseline or counterfactual values. For example, in patients with a history of cardiovascular disease (CVD), an intervention may have the potential to avoid a stroke. To model the benefits of avoiding a stroke, the analyst would ideally require a mean utility value from a cohort of patients who have recently experienced a stroke (plus follow-up data) and a mean utility value from a cohort who have not experienced a stroke but do have a history of CVD. Another example would be a screening programme for hearing impairment. In this instance, analysts would need the mean utility value from a cohort with hearing impairment (plus follow-up data to capture potential changes in HRQoL over time) and a mean utility value from a cohort without a history of hearing impairment. Our study provides utility estimates for self-reported chronic conditions and

for respondents with ADL limitations, these values could be used for the calculation of quality-adjusted life years (QALYs) for cost-effectiveness analysis.

Conclusion

Singapore is countering ageing by rolling out several active aging initiatives to enhance the quality of life of elderly. At this juncture, this study has identified significant predictors of HRQoL in elderly Singapore residents, which are potential targets for active aging interventions. The study also provides community-based EQ-5D index and VAS scores associated with a wide variety of chronic conditions and ADL limitations, these can be used to estimate quality-adjusted life-years in cost-effectiveness analyses.

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Wake-up Stroke and Onset-to-door Duration Delays: Potential Future Indications for Reperfusion Therapy

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Abstract

Introduction: There is limited utilisation of acute stroke reperfusion treatments which have narrow therapeutic windows, with delayed hospital presentation being a major limiting factor in Singapore. Most patients who wake up with symptoms are ineligible for reperfusion treatments as duration from onset time is not known. We studied the profile of wake-up strokes, onset-to-door duration and their associated factors among ischaemic stroke patients in the context of potential new treatments. **Materials and Methods:** This is an observational study of consecutive ischaemic stroke patients presenting within 2 weeks of symptom onset to the Singapore General Hospital in 2012. **Results:** Of the 642 ischaemic stroke patients studied, 33% of the cases were wake-up strokes [median age 64 years, 88% <80 years; median NIHSS score 4, 98% <20]. The median onset-to-door duration was 14.3 hours (Interquartile range, 4.8 to 38.2 hours), 20% of them arrived <3.5 hours (considering eligibility for intravenous alteplase in the proven 4.5 hours window accounting for a one hour door-to-needle duration), 14%: ≥3.5 to <8 hours, 11%: ≥8 to <12 hours, and 56%: ≥12 hours. Most patients with known stroke risk factors including atrial fibrillation (66%), hypertension (78%) and prior stroke (81%) presented beyond 3.5 hours. **Conclusion:** The one-third proportion of wake-up stroke in this cohort and low prevalence of relative contraindications suggest this is a promising group for emerging thrombolysis indications. With the majority of patients presenting after 8 hours, widening of the therapeutic window with new potential reperfusion treatments would not appreciably increase treatment utilisation. This study reaffirms the urgent need for public education to improve stroke awareness in Singapore.

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Key words: Hospital presentation, Ischaemic stroke, Stroke awareness

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Introduction

In ischaemic stroke, acute reperfusion therapy aims to recanalise arterial obstruction leading to salvage of hypoperfused cerebral tissue with the goal of improving clinical outcomes.¹ Reperfusion treatments include intravenous thrombolysis with alteplase which is licensed within the narrow therapeutic window of 4.5 hours,² novel intravenous fibrinolytics which are under trial,³ and interventions such as intra-arterial thrombolysis and mechanical thrombectomy which are currently not licensed for acute stroke treatment.⁴ Worldwide, utilisation of reperfusion therapies is low, with only 2% to 4% of ischaemic stroke patients receiving intravenous thrombolysis.⁵ Similarly in Singapore, less than 5% of ischaemic stroke patients receive intravenous thrombolysis, with the main limitation being presentation beyond the

therapeutic time window.⁶ In addition, stroke patients who wake up with neurological deficits (wake-up strokes) are a therapeutic dilemma. As their stroke onset time is unknown, they are often ineligible for intravenous thrombolysis and studies have reported lower recanalisation rates and worse functional outcomes.⁷

Currently, there are no published data on wake-up strokes in Singapore. Prior studies on onset-to-door duration for stroke in Singapore did not consider wider time frames. We aimed to identify the future potential indications for reperfusion therapy such as wider time windows and imaging surrogates for stroke duration in unknown stroke onset, as well as to determine if the onset-to-door duration has improved since prior surveys. Thus, we studied the prevalence and profile of wake-up strokes, onset-to-door duration following stroke onset and patient characteristics

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associated with presentation delay among ischaemic stroke patients presenting to the Singapore General Hospital (SGH).

Materials and Methods

We conducted an observational cross-sectional study of consecutive ischaemic stroke patients who presented to SGH over one year in 2012. Data were collected from a hospital-based audit of all ischaemic stroke cases. The inclusion criterion was acute ischaemic stroke based on clinical findings and brain imaging with symptom onset within 2 weeks. Patients with haemorrhagic stroke and those who were not able to determine whether stroke onset occurred during sleep or while awake were excluded. Time of stroke onset was defined as when the stroke symptoms first started, or when the patient was last seen well in wake-up strokes. Time of hospital presentation was as noted by arrival to the emergency department. We also collated stroke severity at presentation using the National Institutes of Health Stroke Score (NIHSS) score,⁸ stroke subtype using the Oxfordshire Community Stroke Project (OCSP) classification,⁹ and risk factors including hypertension, diabetes, hyperlipidemia, smoking status, previous stroke, atrial fibrillation, and ischaemic heart disease. Accounting for an 1-hour door-to-needle duration, we selected 4 time frames of onset-to-door duration, <3.5 hours (based on 4.5 hours window for intravenous alteplase), ≥3.5 to <8 hours (based on potential wider time windows for novel fibrinolytics such as tenecteplase and desmoteplase, as well as interventional treatment such as intra-arterial thrombolysis and mechanical thrombectomy), ≥8 to <12 hours and ≥12 hours.

Statistical analyses were carried out using SPSS version 20.0.0 (SPSS Inc, Chicago, IL). We performed chi-square statistical test for categorical variables and Mann-Whitney test for continuous variables. This study was approved for consent waiver by the hospital's Institutional Review Board.

Results

Of the 815 ischaemic stroke patients admitted to the Singapore General Hospital in 2012, 642 (79%) patients fulfilled the inclusion criteria for this study. Wake-up strokes made up 33% (213) of the 642 acute ischaemic stroke patients studied, and had a median age of 64 years (IQR, 56 to 74 years), with 88% of the patients were younger than 80 years old and 64% of them were male. The median NIHSS score was 4 (IQR, 2 to 8), with 98% having a score of <20. The OCSP distribution was 3.4% of the total anterior circulation infarct (TACI), 19.2% partial anterior circulation infarct (PACI), 12.1% posterior circulation infarct (POCI) and 65.3% lacunar infarct (LACI). A significantly higher proportion of wake-up stroke patients presented beyond

3.5 hours compared to stroke while awake patients (97% vs 72%, $P < 0.001$). Patients with wake-up stroke and those with stroke while awake were similar in terms of age, gender, stroke subtype and risk factor distribution (Table 1).

The median onset-to-door duration was 860 minutes (14 hours and 20 minutes) (IQR 288 to 2289 minutes), with 20% of patients presenting <3.5 hours, 14% ≥3.5 to <8 hours, 11% ≥8 to <12 hours, and 55% ≥12 hours. The majority presented beyond 3.5 hours (80%), even among those with known risk factors of stroke, such as atrial fibrillation (66%), hypertension (78%) and prior stroke (81%). There was a higher proportion of patients aged >80 years (19% vs 10%, $P = 0.006$), with atrial fibrillation (20% vs 10%, $P = 0.001$) and non-smokers (83% vs 70%, $P = 0.011$) among those

Table 1. Profile of Ischaemic Stroke Patients by Wake-up Stroke or Stroke While Awake (n = 642)

	Wake-up Stroke (n = 213)	Stroke While Awake (n = 429)	P value*
Median age, years (IQR)	64 (56 – 74)	65 (57 – 74)	0.619
Age <80 years, n (%)	188 (88.3)	379 (88.3)	0.976
Male, n (%)	136 (63.8)	273 (66.7)	0.958
Median NIHSS (IQR)	4 (2 – 8)	3 (1 – 7)	0.012
NIHSS <20, n (%)	198 (97.5)	385 (97.2)	0.821
OCSP, n (%)			
TACI	6 (2.8)	16 (3.7)	0.664
PACI	36 (16.9)	87 (20.3)	
LACI	145 (68.1)	274 (63.9)	
POCI	26 (12.2)	52 (12.1)	
Hypertension, n (%)	139 (65.3)	310 (72.3)	0.068
Diabetes, n (%)	89 (41.8)	166 (38.7)	0.451
Hyperlipidaemia, n (%)	128 (60.1)	278 (64.8)	0.244
Previous stroke, n (%)	44 (20.7)	95 (22.1)	0.667
Atrial fibrillation, n (%)	25 (11.7)	51 (11.9)	0.956
Ischaemic heart disease, n (%)	50 (23.5)	97 (22.6)	0.806
Current smoking, n (%)	55 (25.8)	122 (28.4)	0.399
Time from onset/last seen well to door, n (%)			
<3.5 hours	7 (3.3)	122 (28.4)	<0.001
≥3.5 hours	206 (96.7)	307 (71.6)	

*P value based on chi-square statistical test for categorical variables and Mann-Whitney test for continuous variables.

IQR: Interquartile Range; NIHSS: National Institutes of Health Stroke Score; TACI: Total Anterior Circulation Infarction; PACI: Partial Anterior Circulation Infarction; LACI: Lacunar Infarction; POCI: Posterior Circulation Infarction; OCSP: Oxfordshire Community Stroke Project

Table 2. Factors Associated with Hospital Presentation Duration <3.5 or ≥3.5 hours (n = 642)

	<3.5 hrs (n = 129)	≥3.5 hrs (n = 513)	P value*
Age ≤80 years, n (%)	105 (81.4)	462 (90.0)	0.006
>80 years, n (%)	24 (18.6)	51 (10.0)	
NIHSS <20, n (%)	124 (96.1)	502 (97.9)	0.256
NIHSS ≥20, n (%)	5 (3.9)	11 (2.1)	
Hypertension, n (%)	99 (76.7)	350 (68.2)	0.059
No hypertension, n (%)	30 (23.3)	163 (31.8)	
Diabetes, n (%)	50 (38.8)	205 (40.0)	0.803
No diabetes, n (%)	79 (61.2)	308 (60.0)	
Hyperlipidaemia, n (%)	89 (69.0)	317 (61.8)	0.130
No hyperlipidaemia, n (%)	40 (31.0)	196 (38.2)	
Previous stroke, n (%)	27 (20.9)	112 (21.8)	0.824
No previous stroke, n (%)	102 (79.1)	401 (78.2)	
Atrial fibrillation, n (%)	26 (20.2)	50 (9.7)	0.001
No atrial fibrillation, n (%)	103 (79.8)	463 (90.3)	
Ischaemic heart disease, n (%)	37 (28.7)	110 (21.4)	0.080
No ischaemic heart disease, n (%)	92 (71.3)	403 (78.6)	
Current/Past smoker, n (%)	22 (17.1)	155 (30.2)	0.011
Non-smoker, n (%)	107 (82.9)	358 (69.8)	

*P value based on chi-square statistical test for categorical variables.

NIHSS: National Institutes of Health Stroke Score

who presented within 3.5 hours versus beyond 3.5 hours. Stroke severity (NIHSS ≥20), previous stroke, hypertension, diabetes, hyperlipidaemia, and ischaemic heart disease were not associated with delayed presentation beyond 3.5 hours (Table 2). After adjustment of variables with $P < 0.1$ (namely age more or less than 80 years, hypertension, atrial fibrillation, ischaemic heart disease and smoking status), only age >80 years ($P = 0.043$) and atrial fibrillation ($P = 0.008$) were independently associated with hospital presentation within 3.5 hours.

Discussion

In our ischaemic stroke cohort, one-third of the patients were wake-up strokes, similar to published reports ranging from 14% to 28%.^{10,11} The majority of wake-up strokes presented more than 3.5 hours from the time they awoke with stroke symptoms, and hence beyond the current time indications for intravenous thrombolysis, given an estimated one hour door-to-needle time. Most wake-up stroke patients did not have relative contraindications to intravenous thrombolysis, namely TACI, severe neurological deficit (NIHSS ≥20), and old age (≥80 years).^{2,12} Thus, wake-up strokes in Singapore is a promising subgroup for future indications of reperfusion therapies such as extended time

windows for intravenous thrombolysis with alteplase and newer fibrinolytics, as well as interventional treatments.^{4,13-15}

There are also new possibilities for assessment of wake-up strokes with ongoing randomised trials using imaging surrogates for duration of stroke onset such as diffusion-weighted imaging-fluid-attenuated inversion recovery (DWI-FLAIR) mismatch patterns on MRI in such patients with unknown onset.^{16,17}

Only one-fifth of ischaemic stroke patients presented within the 3.5-hours thrombolytic time frame, and an additional small proportion (14%) presented within the extended ≥3.5 to <8 hour time window. Hence, even if ongoing trials such as EXtending the time for Thrombolysis in Emergency Neurological Deficits (EXTEND) and Desmoteplase in Acute Ischaemic Stroke 3 (DIAS-3) trials prove the safety and efficacy of reperfusion therapies at extended times,^{14,15} widening of the therapeutic window to 9 hours would not increase utilisation of reperfusion therapies appreciably in Singapore.

As the majority of patients presented considerably beyond current and possible future therapeutic windows, the key to increasing utilisation of reperfusion treatments is reducing the onset-to-door duration. It has been estimated that up to 24% of stroke patients are eligible for thrombolytic treatment should delayed onset-to-door presentation be avoided.¹⁸ In a review of hospital presentation following stroke around the world, the median onset-to-door duration was 3 to 4 hours, with Singapore faring very poorly in comparison.¹⁹ Furthermore, there has been minimal improvement in hospital presentation following stroke with similar median onset-to-door duration in this 2012 study (14 hours 20 minutes) compared to our 2004 hospital-based survey (16 hours 5 minutes).⁶

These data suggest an urgent need for more effective public health education strategies to reduce the onset-to-door presentation in Singapore. Studies have shown that provision of stroke information alone, without education on the severity of stroke and possibility of time-dependent acute treatment, does not change health-seeking behaviours and decrease onset-to-door presentation time.²⁰⁻²² As such, stroke education strategies should focus on both recognition of stroke symptoms and awareness of the urgent need to present expediently to hospital. A survey done by our group in 2009 showed that the main reasons cited for a delay in hospital presentation were that patients did not realise the gravity of their symptoms or did not recognise them as stroke.²³ Furthermore, our study showed most patients with known risk factors of stroke had delayed hospital presentation, such as those with hypertension and atrial fibrillation who are thus important target groups for stroke awareness education. Of note, the majority of patients with previous stroke presented beyond the current

treatment window, indicating a missed opportunity for stroke education during prior medical consultation.

The main strength of this study is the use of a hospital-wide audit database which prospectively captures all stroke admissions over the year, preventing patient selection bias. As the study was limited to a single tertiary hospital in Singapore, the data may however be subjected to hospital bias. However, in view of the small size of our nation with relative homogenous distribution of the population, it is expected that these results are representative of Singapore public hospitals in general.

Conclusion

In conclusion, wake-up strokes form one-third of all ischaemic strokes in Singapore, and are a potential subgroup for new indications for reperfusion treatments currently under investigation. As the majority of stroke patients have very delayed hospital presentation, widening the time window of reperfusion therapies will not appreciably increase its utilisation in our current Singapore context. Our findings emphasise the urgent need for public stroke education, especially in high-risk groups, to reduce hospital presentation delays and thereby increase eligibility for acute stroke reperfusion treatments proven to improve patient outcomes.

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Normative Data for the Singapore English and Chinese SF-36 Version 2 Health Survey

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Abstract

Introduction: The aim of this study is to report normative data for the Short-Form 36 version 2 (SF-36v2) for assessing health-related quality of life, in the Singapore general population. **Materials and Methods:** Data for English and Chinese-speaking participants of the Singapore Prospective Study Programme were analysed. The SF-36v2 scores were norm-based with the English-speaking Singapore general population as reference and reported by age (in decades), gender and ethnicity as well as for the 5 most prevalent chronic medical conditions. Scores were reported separately for the English and Chinese language versions. **Results:** A total of 6151 English-speaking (61.5% Chinese and 19.2% Malay) and 1194 Chinese-speaking participants provided complete data. Mean (SD) age of all participants was 49.6 (12.58) years with 52.4% being women. In both languages, women reported lower scores than men on all scales. Among the chronic medical conditions, stroke had the largest impact on all English SF-36v2 scales and on 3 Chinese SF-36v2 scales (role-physical, general health and social functioning). **Conclusion:** We have provided detailed normative data for the Singapore English and Chinese SF-36v2, which would be valuable in furthering HRQoL research in Singapore and possibly the region.

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Key words: Health-related quality of life, Health status, Mental well-being, Social well-being

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Introduction

Health-related Quality of Life (HRQoL) measures are increasingly being incorporated into clinical research and practice as a tool to understand, from the patients' perspective, the impact of a disease on their physical, mental and social well-being. The Medical Outcomes Short-Form 36 (SF-36) Questionnaire is arguably the most commonly used generic profile-based HRQoL measure, with translations in over 120 languages across more than 40 countries.¹

The SF-36 version 2 (SF-36v2) was developed to overcome some of the deficiencies in the original version (henceforth referred to as version 1, v1).¹ Revisions to the SF-36v1 may be summarised as (i) simpler instructions and improved layout for questions and answers to improve clarity, (ii) improved phrasing of some items to provide greater comparability with translations and cultural

adaptations widely-used in the United States (US) and in other countries, and (iii) revision of response options from dichotomous to 5-level response choices for the role physical and role emotional items to improve sensitivity, and from 6-level to 5-level response choices for the vitality and mental health items for simplification.¹

The normative data of the SF-36v1 for the Singaporean general population were previously reported² and have since been used in clinical research in Singapore, including a 2-year prospective longitudinal study to evaluate health outcomes in osteoarthritis patients after total knee replacement³ and several cross-sectional studies evaluating HRQoL in thyroid cancer survivors,⁴ chronic hepatitis B infections⁵ and stroke survivors.⁶ The purpose of this paper is to report the normative data for the SF-36v2 in the Singapore general population, in the hope that this will similarly be useful for clinical research in Singapore.

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Materials and Methods

Study Design and Participants

Data for this Institutional Review Board-approved study were collected as part of the Singapore Prospective Study Programme (SP2). SP2 is a cross-sectional study that involves a follow-up of 10,747 participants from 4 previous cross-sectional surveys (from 1982 to 1998). Participants were invited to participate in this follow-up examination conducted between 2004 and 2007, where HRQoL data including the SF-36v2 were collected for the first time. Written informed consent was obtained from all participants prior to commencing the study.

Detailed sample selection methods for the original studies have been described elsewhere and include the Thyroid and Heart Study (1982 to 1984),⁷ the National Health Survey (1992),⁸ the National University of Singapore Heart Study (1993 to 1995)⁹ and the National Health Survey (1998).⁸ Briefly, all studies were a random sample of participants from the Singapore population, with disproportionate sampling stratified by ethnicity to increase the number of minority ethnic participants (Malays and Asian Indians). Using the unique National Registration Identity Card numbers, the Ministry of Home Affairs provided current addresses and phone numbers of participants. Participants were then contacted by either mail or telephone to obtain an appointment for trained field interviewers to administer questionnaires at the participant's home. Three home visits were made on 3 different times of the day, including at least 1 weekend and 1 weekday, before a participant was deemed non-contactable. All interviewed participants were subsequently invited to attend a clinical examination for additional tests and collection of biological specimens, shortly after the home visit.

Data Collection

Interviewers collected data on medical history, demographic and lifestyle (alcohol intake, smoking) factors using a pre-tested questionnaire. Participants were classified as being Chinese, Malay or Asian Indian according to self-report. Age was calculated based on self-reported date of birth. History of chronic diseases was captured by self-report and a few of these were confirmed by laboratory data. Participants were asked whether they had ever been told that they had hypertension, diabetes mellitus or high cholesterol. History of coronary heart disease was defined as a positive response to any of the 3 questions 'Has your doctor ever told you that you have blockage of the arteries to your heart?' or 'Have you had ever had a heart attack?' or 'Have you ever had angioplasty-ballooning or heart bypass operation procedures?' Participants were also asked whether they had ever been told by a physician that they had a cerebrovascular accident (i.e. stroke). Information on other chronic diseases

(lung disease, cancer, musculoskeletal illness and mental illness) was also captured using a checklist. The presence of hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mm Hg or history of hypertension. The presence of diabetes mellitus was defined as patients with a fasting glucose level ≥ 7.0 mmol l⁻¹ or with a known history of diabetes mellitus or those currently taking antidiabetic medications. Participants were classified as having dyslipidaemia if they have met any of the following two criteria: participant answered 'yes' to the question 'Are you taking any medication for high cholesterol?'; fasting total cholesterol 6.2 mmol l⁻¹ or more; low-density lipoprotein cholesterol 4.1 mmol l⁻¹ or more; high-density lipoprotein cholesterol less than 1.0 mmol l⁻¹; or fasting triglyceride 2.3 mmol l⁻¹ or more using National Cholesterol Education Program Adult Treatment Panel III (NCEPATP III) clinical cutoff points for lipid parameters.¹⁰ For the health examination, participants were examined in the morning after a 10-hour overnight fast. Details of health examination, blood draw, sample preparation and biochemical analyses were previously published.¹¹

Short-Form 36 Health Survey Version 2 (SF-36v2)

The SF-36v2 is an improvement over the original version and is a generic HRQoL instrument comprising 36 items measuring 8 domains, namely, physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE) and mental health (MH), with higher scores reflecting better perceived health.¹ The SF-36v2 uses norm-based scoring algorithms (T-score transformation with mean of 50 and standard deviation of 10) for all 8 scales. For example, an individual with a score of 40 on the PF indicates that he or she had worse PF by one standard deviation compared to the general population. Two summary scores, physical component summary (PCS) and mental component summary (MCS), may be computed on the basis of the 8 domain scores using regression weights derived from principal component factor analysis with varimax rotation. The reliability and validity of the SF-36v2 in Singapore were reported separately.¹²

Statistical Analyses

Data were first entered into an Excel spreadsheet (Microsoft Corporation) and subsequently converted to Stata format using StatTransfer (Circle Systems). Individual SF-36v2 items were recoded, summed and transformed, with missing values imputed as recommended in the SF-36v2 user manual.¹³ The reference group used in norm-based scoring is the English-speaking Singapore general population rather than the US general population. Participants with missing scale scores were excluded listwise from analysis.

Study participants analysed were classified into subgroups stratified by age (in decades, starting from 21 years), gender (men and women) and ethnicity (Chinese/ Malay/ Indians). In addition, we classified participants into groups with and without a specific chronic medical condition. Due to the large number of chronic medical conditions captured in this study, we limited the reporting of SF-36v2 scores to the 5 most prevalent chronic medical conditions.

In Singapore, the SF-36v2 is available in English, Chinese, Malay and Tamil. In this study, we have analysed the data for only the English and Chinese language versions of the SF-36v2 due to the small number of study participants who completed the survey in Malay and Tamil ($n = 227$). Data were analysed separately for the English and Chinese language surveys. As participants who completed the English SF-36v2 (multi-ethnic) were clearly different from those who completed the Chinese SF-36v2 (Chinese only), we did not perform any statistical tests of comparisons between the 2 groups of participants. However, we did compare the characteristics of English- and Chinese-speaking Chinese. All data analyses were performed using Stata version 10 (StataCorp LP).

Results

Characteristics of Study Participants

Out of 10,747 participants available for follow-up, complete data for 7345 participants (68.3%) were eventually analysed, among whom, 6151 completed the SF-36v2 in English while 1194 completed the SF-36v2 in Chinese. In all, 2580 participants did not return for clinic examination and were excluded when computing the normative data

for selected chronic medical conditions. This was because we would like to use a combination of self-reported and laboratory confirmed data for chronic medical conditions. Reasons for exclusion of other participants are detailed in Figure 1. In the analysed sample of 7345 participants, the mean (SD) age of participants was 49.6 (12.58) years, 3848 (52.4%) were women, 4974 (67.7 %) were Chinese and 1182 (16.1 %) were Malay. Distribution of participant characteristics by language is given in Table 1. Chinese SF-36v2 scores were computed with reference to the English-speaking Singapore population and are generally lower compared to the English SF-36v2 although the differences were small (range of score differences: 1.03 to 2.53). Compared to Chinese-speaking Chinese, English-speaking Chinese participants were younger on average (mean (SD) age, years 55.6 (11.16) vs 47.8 (12.58), $P < 0.001$), more likely to be men, have lower prevalence of chronic medical conditions and higher SF-36v2 scores (Table 1). Among the English speakers, Indians were significantly older with mean (SD) age for Chinese, Malays and Indians being 47.8 years (12.58), 47.9 years (12.37) and 50.9 years (12.07), respectively. The distribution of overall English and Chinese SF-36v2 scale scores are given in Figures 2 and 3, respectively.

SF-36v2 Norms for Singapore

The English SF-36v2 norms stratified by age, gender and ethnicity are summarised in Table 2. In general, women reported lower scores than men on all scales and across the 3 ethnicities. At the same time, Indians generally reported lower scores on all scales. English-speaking Chinese

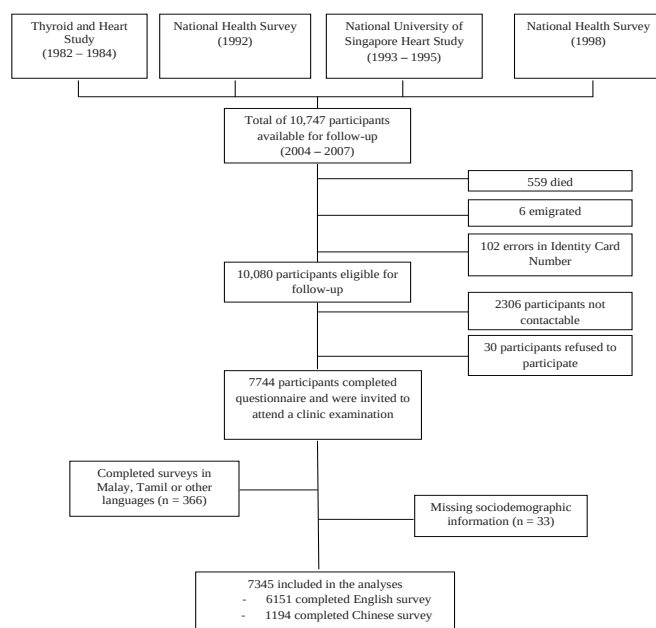


Fig. 1. Flow chart of study participants.

Table 1. Characteristics of Study Participant by Survey Language

	Completed English SF-36v2					Completed Chinese SF-36v2	
	All (n = 6151)	Chinese (n = 3780)	Malay (n = 1182)	Indian (n = 1189)	P value (among ethnic groups)	(n = 1194)	P value (between English and Chinese-speaking ethnic Chinese)
Mean (SD) Age, years	48.4 (12.51)	47.8 (12.58)	47.9 (12.37)	50.9 (12.07)	<0.001	55.6 (11.16)	<0.001
Age, years, n (%)							
≤40	1592 (25.9)	1090 (28.8)	294 (24.9)	208 (17.5)	<0.001	79 (6.6)	<0.001
41 to 50	2028 (33.0)	1204 (31.9)	430 (36.4)	394 (33.1)		318 (26.6)	
51 to 60	1485 (24.1)	856 (22.6)	278 (23.5)	351 (29.5)		396 (33.2)	
>60	1046 (17.0)	630 (16.7)	180 (15.2)	236 (19.9)		401 (33.6)	
Women, n (%)	3162 (51.4)	1941 (51.4)	598 (50.6)	623 (52.4)	0.675	686 (57.5)	<0.001
Five most prevalent chronic medical conditions, n (%)							
Dyslipidaemia	1783 (29.0)	937 (24.8)	382 (32.3)	464 (39.0)	<0.001	373 (31.2)	<0.001
Hypertension	1593 (25.9)	926 (24.5)	315 (26.7)	352 (29.6)	<0.001	400 (33.5)	<0.001
Diabetes mellitus	634 (10.3)	242 (6.4)	153 (12.9)	239 (20.1)	<0.001	142 (11.9)	<0.001
Coronary heart disease	175 (2.8)	75 (2.0)	23 (2.0)	77 (6.5)	<0.001	32 (2.7)	0.150
Stroke	87 (1.4)	38 (1.0)	10 (0.9)	39 (3.3)	<0.001	29 (2.4)	<0.001
Mean (SD) SF-36v2 Norm-based Scores*							
Physical Functioning	50 (10)	51.09 (9.10)	49.61 (10.24)	46.94 (11.69)	<0.001	48.81 (9.89)	<0.001
Role-Physical	50 (10)	51.08 (8.94)	49.17 (10.33)	47.38 (12.07)	<0.001	48.26 (10.40)	<0.001
Bodily Pain	50 (10)	52.09 (9.14)	49.49 (9.92)	47.04 (11.90)	<0.001	48.97 (10.56)	<0.001
General Health	50 (10)	50.18 (9.74)	50.42 (10.07)	49.01 (10.65)	>0.001	47.51 (11.73)	<0.001
Vitality	50 (10)	50.01 (9.98)	50.70 (9.25)	49.27 (10.71)	<0.001	47.47 (10.75)	<0.001
Social Functioning	50 (10)	50.84 (9.12)	49.66 (10.26)	47.67 (11.85)	<0.001	48.78 (10.10)	<0.001
Role-Emotional	50 (10)	50.75 (9.16)	49.76 (9.94)	47.87 (12.09)	<0.001	48.70 (10.53)	<0.001
Mental Health	50 (10)	50.23 (9.64)	50.76 (9.63)	48.51 (11.28)	<0.001	47.78 (10.76)	<0.001

*The reference population is the multi-ethnic English-speaking Singapore general population.

men aged 21 to 40 years reported the lowest mean (SD) VT scores of 49.86 (10.52) compared to Chinese men of other ages (range, 51.50 to 52.41). A different trend was observed among English-speaking Malay and Indian men, with those aged 60 years and older reporting the lowest VT scores compared to other ages (Table 2). Among English-speaking women, there was a clear trend of decreasing PF with increasing age in all ethnicities (Table 2) with the differences across age categories being largest among the English-speaking Indian women where the difference in mean PF scores for participants 21 to 40 years old and those older than 60 years was 10.6. Interestingly, on several scales, the differences in SF-36v2 scores between men and women were generally smaller among Chinese compared to Malays and Indians. For example, the difference in BP scores between Chinese men and women, between Malay men and women and between Indian men and women were 1.58, 2.37 and 4.56, respectively. The Chinese SF-36v2 norms stratified by age and gender are summarised in Table 3. Chinese-speaking women reported lower scores than Chinese-speaking men on all SF-36v2 scales.

SF-36v2 Scores in Participants with Diabetes, Hypertension, Dyslipidaemia, Coronary Heart Disease or Stroke

Dyslipidaemia (29.0%), hypertension (25.9%), diabetes mellitus (10.3%), coronary heart disease (2.8%) and stroke (1.4%) were the 5 most prevalent chronic medical conditions among English-speaking participants in this study. The same 5 conditions were most prevalent among Chinese-speaking study participants except that hypertension (33.5%) was more prevalent than dyslipidaemia (31.2%). SF-36v2 norms for participants with and without these chronic medical conditions for the English and Chinese surveys are summarised in Tables 4 and 5, respectively. Among English-speaking participants, those with stroke reported the lowest SF-36v2 scores on all scales compared to participants with other chronic medical conditions. The score difference among the chronic medical conditions was largest (14.19) for the PF scale where mean (SD) PF scores was highest at 48.52 (10.72) for participants with dyslipidaemia and lowest at 34.33 (16.77) for participants with stroke. Among Chinese-speaking participants, those

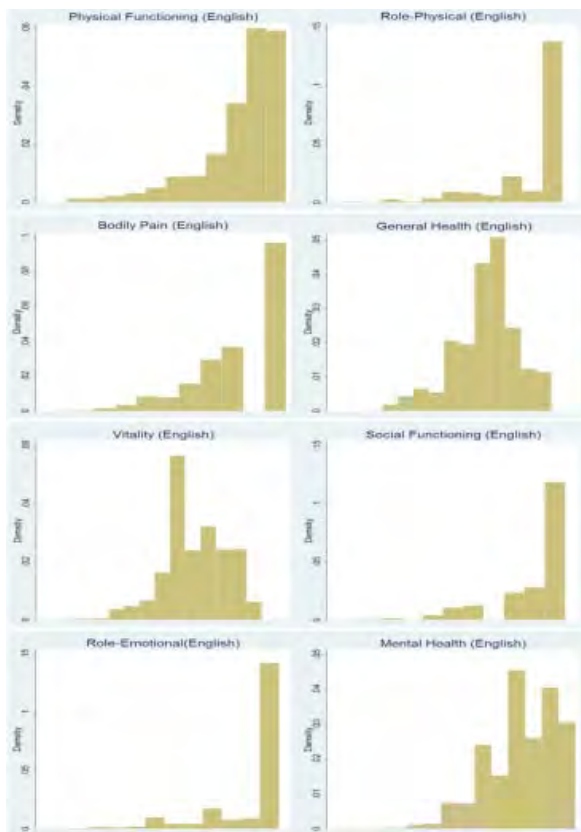


Fig. 2. Distribution of English (Singapore) SF-36v2 norm-based scores by scales.

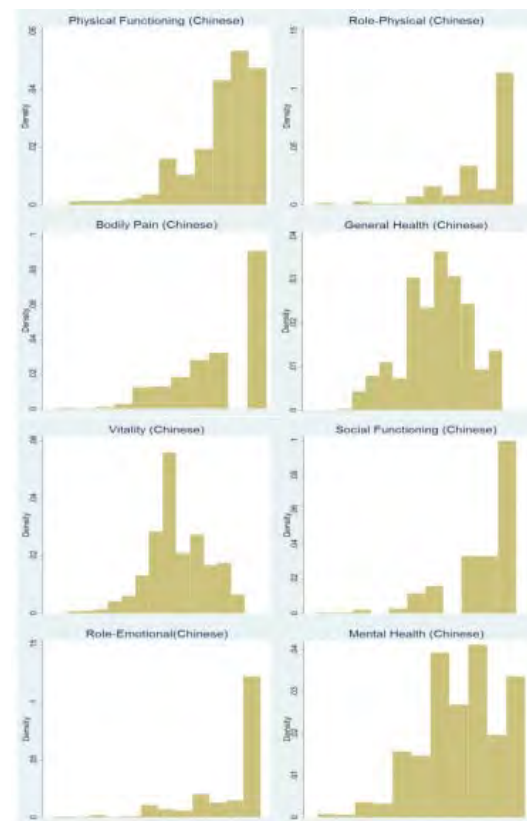


Fig. 3. Distribution of Chinese (Singapore) SF-36v2 norm-based scores by scales.

with coronary heart disease ($n = 32$) reported the lowest scores on 4 of 8 scales (PF, BP, RE and MH) whereas those with stroke ($n = 29$) reported the lowest scores on the remaining 4 scales (RP, GH, VT and SF). Chinese-speaking participants with diabetes mellitus reported the lowest scores on GH.

Discussion

This paper presents the normative data for the SF-36v2, an update from our earlier publication on the SF-36v1.² To facilitate comparison with the earlier paper, we have organised the results as similarly as possible, i.e. stratified by age, gender and ethnicity in the English-speaking group and by age and gender in the Chinese-speaking group. However, the age categories were organised differently because there were very few Chinese-speaking individuals who are aged 21 to 40 years. In the earlier paper, age categories were 21 to 30, 31 to 40, 41 to 50 and ≥ 51 . Hence, age-specific comparison between the 2 papers can only be made for the other 2 categories (41 to 50 years and 51 years and above). The resulting sample is similar in age characteristics with

the Singapore general population. Percent population aged 20 to 64 was 87.1% in the Singapore general population compared with 86.5% in our sample. Percent population aged 65 years and older was 12.9% in the Singapore general population compared with 13.5% in our sample. However, the resulting sample is a slight over representation of Malays and substantial over representation of Indians. The percentage of Chinese, Malays and Indians in the Singapore general population and in the sample were 74.1%, 13.4% and 9.2% versus 67.7%, 16.1% and 16.2%, respectively.

We observed that Indians generally reported lower scores on all scales. This might be because the Indians were older, had a higher proportion of women and had higher prevalence of chronic medical conditions compared to Chinese and Malays. We have also presented the SF-36v2 scores for the 5 most common chronic medical conditions observed in this set of data. Unlike our previously reported study of the SF-36v1 which used self-reported chronic medical condition data, the present study used a combination of laboratory tests and self-reports in defining the presence of chronic medical conditions. As may be expected, SF-36v2

Table 2. Mean (SD) English (Singapore) SF-36v2 Norms by Age, Gender and Ethnicity (n = 6151)

Age group, years	Males					Females					
	All	21 – 40	41 – 50	51 – 60	≥60	All	21 – 40	41 – 50	51 – 60	≥60	All
Chinese	n = 3780	n = 512	n = 597	n = 416	n = 314	n = 1839	n = 578	n = 607	n = 440	n = 316	n = 1941
PF	51.49 (8.97)	54.16 (7.61)	53.68 (7.59)	52.82 (7.76)	48.24 (10.91)	52.69 (8.54)	53.32 (7.02)	51.72 (7.77)	49.10 (9.29)	44.02 (11.55)	50.35 (9.21)
RP	51.57 (8.72)	52.01 (8.56)	53.07 (7.00)	52.17 (8.34)	49.55 (10.89)	51.97 (8.58)	52.20 (7.52)	52.29 (7.63)	51.33 (9.03)	47.09 (11.43)	51.20 (8.84)
BP	51.40 (8.98)	52.38 (8.99)	52.43 (8.06)	52.14 (8.53)	51.59 (8.85)	52.21 (8.57)	51.67 (8.95)	50.93 (9.04)	50.25 (9.16)	48.70 (10.20)	50.63 (9.29)
GH	50.53 (9.37)	51.50 (9.14)	51.53 (8.67)	51.67 (8.98)	49.03 (10.02)	51.13 (9.15)	51.46 (8.59)	51.32 (8.67)	48.99 (9.95)	45.99 (10.91)	49.97 (9.55)
VT	50.42 (9.81)	49.86 (10.52)	51.50 (8.76)	52.41 (9.01)	51.76 (9.54)	51.29 (9.51)	48.60 (10.50)	50.68 (9.54)	50.38 (9.72)	48.29 (10.11)	49.60 (10.02)
SF	51.18 (9.01)	50.59 (9.56)	52.22 (7.84)	51.75 (8.43)	50.94 (9.57)	51.44 (8.80)	50.65 (9.20)	51.69 (8.44)	51.87 (8.82)	48.67 (10.68)	50.93 (9.21)
RE	51.12 (8.95)	50.62 (9.36)	52.10 (7.49)	52.01 (8.15)	50.61 (10.19)	51.41 (8.70)	50.21 (9.15)	51.59 (8.26)	51.92 (8.61)	49.03 (11.12)	50.84 (9.17)
MH	50.60 (9.42)	48.87 (10.35)	50.80 (8.97)	51.80 (8.87)	53.38 (8.68)	50.93 (9.43)	49.01 (10.25)	50.65 (9.36)	51.38 (8.65)	50.45 (8.66)	50.29 (9.41)
Malay	n = 1182	n = 137	n = 214	n = 148	n = 85	n = 584	n = 157	n = 216	n = 130	n = 95	n = 598
PF	50.03 (10.09)	53.94 (8.34)	52.56 (9.63)	52.03 (7.46)	46.84 (11.44)	51.92 (9.37)	50.27 (9.63)	49.33 (9.08)	46.40 (10.65)	44.57 (12.79)	48.18 (10.42)
RP	49.71 (10.07)	51.26 (8.86)	50.82 (9.16)	50.58 (9.29)	49.33 (10.78)	50.65 (9.37)	48.85 (10.88)	49.34 (9.52)	48.39 (11.29)	48.01 (11.75)	48.79 (10.64)
BP	49.83 (9.74)	51.99 (8.67)	51.11 (9.34)	50.88 (8.77)	49.56 (9.30)	51.03 (9.05)	49.93 (9.87)	49.42 (10.15)	47.52 (10.33)	46.40 (10.62)	48.66 (10.25)
GH	50.76 (9.71)	54.03 (7.63)	52.65 (8.69)	51.60 (10.09)	47.42 (10.82)	51.95 (9.38)	51.13 (9.38)	50.25 (9.14)	48.41 (10.82)	47.18 (10.52)	49.59 (9.89)
VT	51.09 (9.09)	53.22 (8.74)	52.41 (8.32)	52.57 (8.77)	50.28 (8.95)	52.33 (8.65)	49.86 (9.32)	49.98 (8.89)	50.11 (10.06)	49.40 (9.49)	49.89 (9.34)
SF	50.02 (10.14)	51.23 (9.15)	51.11 (9.19)	49.88 (10.52)	50.03 (10.53)	50.67 (9.73)	49.00 (10.06)	49.74 (10.10)	49.75 (10.33)	48.70 (12.32)	48.38 (10.50)
RE	50.15 (9.72)	50.87 (9.30)	50.81 (9.15)	50.36 (9.27)	50.94 (9.40)	50.73 (9.23)	48.64 (11.70)	49.82 (9.48)	49.65 (9.51)	50.54 (9.74)	49.59 (10.15)
MH	51.12 (9.42)	52.28 (8.77)	51.25 (9.23)	52.29 (8.92)	53.53 (8.37)	52.09 (8.93)	49.03 (10.79)	49.31 (10.41)	50.71 (9.72)	52.07 (8.57)	50.17 (9.78)
Indian	n = 1189	n = 88	n = 192	n = 161	n = 125	n = 566	n = 120	n = 202	n = 190	n = 111	n = 623
PF	47.40 (11.52)	52.46 (8.80)	51.13 (10.11)	49.47 (10.99)	44.44 (12.27)	49.39 (11.03)	49.79 (10.24)	47.95 (10.69)	44.17 (11.28)	39.19 (12.44)	45.59 (11.67)
RP	47.96 (11.77)	49.49 (11.92)	50.60 (9.36)	49.87 (10.62)	44.81 (14.24)	48.94 (11.53)	49.91 (9.91)	49.20 (11.33)	46.59 (11.21)	40.97 (13.85)	47.07 (11.92)
BP	47.42 (11.69)	51.51 (9.49)	49.94 (10.52)	49.65 (11.19)	48.59 (10.60)	49.81 (10.59)	48.53 (11.98)	46.83 (11.74)	43.41 (11.85)	41.94 (12.72)	45.25 (12.21)
GH	49.40 (10.25)	53.05 (10.14)	50.90 (9.87)	49.92 (10.62)	47.29 (11.42)	50.16 (10.61)	51.28 (8.60)	50.62 (8.81)	47.97 (10.42)	43.76 (10.14)	48.72 (9.87)
VT	49.69 (10.52)	51.75 (10.32)	52.74 (9.00)	51.45 (9.96)	50.27 (11.73)	51.67 (10.15)	49.41 (9.96)	49.71 (10.48)	46.75 (10.71)	44.90 (10.13)	47.89 (10.54)
SF	48.04 (11.71)	49.12 (11.07)	49.38 (11.05)	49.03 (11.05)	48.19 (12.31)	48.98 (11.32)	48.77 (11.44)	48.52 (11.68)	46.80 (11.59)	43.73 (13.21)	47.19 (12.00)
RE	48.30 (11.81)	49.51 (11.13)	50.23 (9.60)	49.56 (10.31)	47.64 (13.16)	49.36 (10.92)	48.43 (11.02)	49.13 (11.13)	46.60 (13.33)	44.18 (14.20)	47.34 (12.50)
MH	48.92 (11.03)	49.02 (11.37)	49.85 (10.41)	50.70 (11.61)	51.21 (9.56)	50.26 (10.74)	48.12 (10.29)	48.88 (10.88)	46.72 (11.68)	46.74 (11.52)	47.69 (11.15)

PF: Physical functioning; RP: Role-physical; BP: Bodily pain; GH: General health; VT: Vitality; SF: Social Functioning; RE: Role-emotional; MH: Mental health

Table 3. Mean (SD) Chinese (Singapore) SF-36v2 Norms by Age and Gender (n = 1194)

Age group, years	Males					Females					
	All	21 – 40	41 – 50	51 – 60	≥60	All	21 – 40	41 – 50	51 – 60	>60	All
	n = 1194	n = 32	n = 119	n = 171	n = 186	n = 508	n = 47	n = 199	n = 225	n = 215	n = 686
PF		55.55 (3.82)	54.35 (5.76)	51.55 (6.73)	46.68 (11.09)		52.64 (7.00)	50.56 (7.77)	49.47 (7.52)	41.26 (12.60)	
RP		51.60 (8.27)	52.07 (7.73)	50.56 (7.75)	45.30 (12.71)		51.36 (8.03)	49.59 (9.06)	48.43 (9.14)	44.29 (12.42)	
BP		52.12 (11.71)	51.24 (9.48)	49.96 (10.12)	49.50 (10.87)		52.23 (7.99)	49.50 (10.14)	47.43 (10.65)	46.40 (11.14)	
GH		52.57 (10.76)	51.62 (9.27)	47.93 (11.31)	46.44 (13.07)		48.93 (9.01)	47.79 (11.08)	47.53 (11.40)	44.46 (12.75)	
VT		49.56 (13.44)	50.39 (9.58)	48.21 (10.46)	47.01 (10.93)		46.99 (10.94)	47.25 (10.39)	46.80 (10.67)	46.36 (11.15)	
SF		50.81 (10.46)	52.77 (7.29)	49.80 (8.08)	47.18 (11.15)		51.05 (8.05)	50.10 (8.77)	49.19 (9.29)	44.73 (12.52)	
RE		51.05 (9.09)	51.13 (8.08)	50.23 (8.47)	46.11 (12.64)		50.86 (7.92)	49.07 (10.33)	48.51 (10.52)	47.41 (11.50)	
MH		49.02 (12.48)	49.20 (10.57)	46.47 (10.50)	48.36 (11.08)		45.05 (11.14)	46.73 (10.20)	47.98 (10.66)	48.70 (10.89)	

PF: Physical functioning; RP: Role-physical; BP: Bodily pain; GH: General health; VT: Vitality; SF: Social Functioning; RE: Role-emotional; MH: Mental health

Table 4. English (Singapore) SF-36v2 Norms in Study Participants with and Without the Stated Chronic Medical Conditions

Chronic medical conditions		Mean (SD) SF-36v2 Norm-based Scores							
		PF	RP	BP	GH	VT	SF	RE	MH
Dyslipidaemia	Y (n = 1783)	48.52 (10.72)	48.78 (11.08)	48.77 (10.50)	49.01 (10.68)	50.33 (9.98)	49.32 (10.42)	49.46 (10.55)	50.55 (9.79)
	N (n = 2546)	50.69 (9.60)	50.46 (9.18)	49.92 (9.82)	51.25 (9.31)	50.32 (10.06)	50.33 (9.60)	49.86 (9.76)	49.90 (10.09)
Hypertension	Y (n = 1593)	48.43 (10.76)	48.99 (10.72)	48.92 (10.37)	49.34 (10.25)	50.77 (9.94)	49.98 (9.84)	49.50 (10.58)	50.88 (9.87)
	N (n = 2520)	51.21 (9.07)	50.61 (9.11)	49.88 (9.85)	51.64 (9.21)	50.38 (9.99)	50.12 (9.77)	49.87 (9.67)	49.80 (10.02)
Diabetes mellitus	Y (n = 634)	45.62 (11.93)	46.41 (12.56)	47.40 (11.50)	45.41 (11.65)	48.47 (10.53)	47.45 (11.75)	48.03 (11.79)	49.86 (10.74)
	N (n = 3678)	50.60 (9.50)	50.41 (9.18)	49.83 (9.81)	51.14 (9.47)	50.63 (9.92)	50.33 (9.53)	50.01 (9.70)	50.19 (9.88)
Coronary heart disease	Y (n = 175)	43.70 (13.04)	43.23 (14.55)	45.98 (12.11)	43.74 (12.63)	47.56 (10.84)	44.74 (13.89)	46.19 (13.43)	49.07 (10.47)
	N (n = 5968)	50.19 (9.83)	50.20 (9.76)	50.13 (9.91)	50.18 (9.85)	50.08 (9.98)	50.15 (9.83)	50.11 (9.87)	50.02 (9.99)
Stroke	Y (n = 87)	34.33 (16.77)	36.83 (17.19)	42.82 (13.35)	42.56 (13.61)	44.58 (14.02)	39.97 (16.74)	41.61 (17.09)	47.29 (13.71)
	N (n = 6064)	50.22 (9.69)	50.19 (9.73)	50.10 (9.91)	50.11 (9.90)	50.08 (9.91)	50.14 (9.80)	50.12 (9.81)	50.04 (9.93)

PF: Physical functioning; RP: Role-physical; BP: Bodily pain; GH: General health; VT: Vitality; SF: Social Functioning; RE: Role-emotional; MH: Mental health; Y: With stated chronic medical conditions; N: Without stated chronic medical conditions

Table 5. Chinese (Singapore) SF-36v2 Norms in Study Participants with and Without the Stated Chronic Medical Conditions

Chronic medical conditions		Mean (SD) SF-36v2 Norm-based Scores							
		PF	RP	BP	GH	VT	SF	RE	MH
Dyslipidaemia	Y (n = 373)	46.49 (11.08)	45.40 (11.86)	45.98 (11.42)	45.51 (12.35)	46.37 (11.53)	46.59 (11.37)	46.29 (12.15)	46.81 (11.66)
	N (n = 484)	50.72 (8.68)	49.23 (9.35)	49.63 (10.29)	49.74 (10.63)	48.70 (10.42)	50.13 (8.77)	48.70 (10.16)	48.49 (10.24)
Hypertension	Y (n = 400)	47.45 (10.56)	46.75 (11.13)	47.11 (11.19)	47.56 (11.36)	47.57 (11.05)	47.63 (10.82)	46.77 (11.54)	47.64 (11.85)
	N (n = 402)	51.30 (8.25)	49.22 (9.30)	48.97 (10.61)	49.89 (10.86)	48.68 (10.93)	50.16 (8.82)	48.91 (9.92)	48.35 (9.97)
Diabetes mellitus	Y (n = 142)	41.87 (12.85)	42.81 (13.25)	45.56 (10.55)	40.71 (13.63)	44.04 (11.34)	43.90 (12.32)	44.97 (13.59)	47.28 (11.54)
	N (n = 711)	50.31 (8.77)	48.59 (9.80)	48.53 (10.88)	49.43 (10.74)	48.58 (10.79)	49.43 (9.55)	48.32 (10.27)	48.02 (10.78)
Coronary heart disease	Y (n = 32)	41.36 (11.83)	39.46 (14.53)	42.99 (12.00)	41.72 (12.02)	45.62 (8.87)	43.63 (11.69)	40.50 (14.20)	44.30 (10.90)
	N (n = 1161)	49.03 (9.75)	48.53 (10.13)	49.15 (10.47)	47.67 (11.69)	47.54 (10.78)	48.92 (10.02)	48.96 (10.27)	47.87 (10.74)
Stroke	Y (n = 29)	41.42 (15.36)	39.16 (15.32)	45.20 (12.72)	40.05 (16.20)	41.60 (11.36)	39.04 (13.34)	42.59 (16.48)	45.91 (11.50)
	N (n = 1165)	49.00 (9.65)	48.49 (10.15)	49.06 (10.49)	47.69 (11.55)	47.62 (10.69)	49.03 (9.89)	48.85 (10.30)	47.82 (10.74)

PF: Physical functioning; RP: Role-physical; BP: Bodily pain; GH: General health; VT: Vitality; SF: Social Functioning; RE: Role-emotional; MH: Mental health; Y: With stated chronic medical conditions; N: Without stated chronic medical conditions

scores were lower among patients with a specific chronic medical condition compared to those without the chronic medical condition.

We noted that the impact of chronic medical conditions on SF-36v2 scores differed among Chinese and English-speaking participants. This could be due to 3 reasons: (i) differences in sociodemographic variables among English and Chinese-speaking participants, (ii) differences in the prevalence of chronic medical conditions among English and Chinese-speaking participants, (iii) language effect due to the use of different language versions of the SF-36v2. As the equivalence of the English and Chinese SF-36v1 has been previously shown,² it is unlikely that the differences were due to the different language versions. However, this remains to be explored in a separate study.

Normative data such as those presented here for the Singapore population by age, gender, ethnicity and chronic medical conditions are important for the meaningful interpretation of results in studies using the SF-36v2 in Singapore in several ways. First, they allow the computation of the expected SF-36v2 scores for Singaporeans adjusted for age, gender, ethnicity and survey language. This would facilitate the interpretation of the SF-36v2 scores obtained in clinical research or routine use with that for the general Singapore population. By observing how the scores for patients involved in clinical trials differ from the general population, this will allow for establishment of

external validity. Second, they facilitate interpretation of the SF-36v2 scores by allowing users to know how their study sample fared compared to the general population of a specific medical condition. For example, if a diabetes mellitus (DM) patient presenting in the clinic reported a PF score of 40, the clinician would know that this patient has a PF score that is one standard deviation below the general DM population in Singapore (mean (SD) PF score: 49.35 (9.70)). Third, they allow identification of specific SF-36v2 domains that are affected by a specific medical condition, thus providing guidance for targeted intervention. For example, English-speaking participants with stroke had the greatest impairment on PF, which is more than one SD below the population norm, compared to other scales. Mean (SD) norm-based scores for SF-36v2 scales among stroke patients were: PF – 34.33 (16.77), RP – 36.83 (17.19), BP – 42.82 (13.35), GH – 42.56 (13.61), VT – 44.58 (14.02), SF – 39.97 (16.74), RE – 41.61 (17.09) and MH – 47.29 (13.71). Note, however, that this comparison across the scales can be done only after the scores were converted to norm-based scoring, which would take into account the arbitrary differences in the ceiling and floor effects for the various SF-36v2 scales.¹² This represents an important advantage of SF-36v2 over SF-36v1.

We recognise that this study is not without its limitations. First, as the presence of chronic medical conditions were based on a combination of laboratory and self-reported

data, participants who did not return for follow-up clinic examination were excluded from the normative data of participants with chronic medical conditions. This resulted in a reduction of available data points as 2580 participants did not return for the clinic examination (24.7%). In our earlier paper,¹¹ we noted that participants who returned for clinic examination were more likely to report better PF, GH, VT and MH, worse BP and RE and similar RP and SF scores. However, as the use of laboratory and self-reported data is more accurate than the use of self-reported data alone, this may represent a pragmatic compromise. In a separate analysis (results available upon request), we computed the norm-based scores using self-reported data alone. The number of participants with self-reported dyslipidaemia, hypertension and diabetes mellitus were fewer than number of participants with these conditions defined by a combination of self-reported and laboratory data. This means that self-reporting underestimated the prevalence of these medical conditions. The definition of coronary heart disease and stroke were based on self-reports only. The general trend was that norm-based scores were lower if medical conditions were determined based on self-reports only. That is, awareness of dyslipidaemia, hypertension and diabetes mellitus was associated with poorer HRQoL. We have made this similar observation in an occupational population in Thailand.¹⁴ However, none of the differences exceeded the clinically important difference of 5 points.

Second, in this study, the SF-36v2 was interviewer-administered. Given that there are documented differences between scores obtained through self- and interviewer-administration,¹⁵ this needs to be borne in mind when comparing scores obtained using a mode of administration other than interviewer-administration. The use of interviewer-administration in this study was necessary so that participants with poor literacy could be included, which has the advantage of providing a more representative assessment of the population as illiterate participants are not excluded.

Third, by combining the 21 to 30 years and 31 to 40 years categories, and by using a combination of laboratory and self-reported data to define chronic medical conditions, we have limited our abilities to directly compare the findings of this study (conducted from 2004 to 2007) with the earlier study (conducted from 1998 to 1999) using the SF-36v1. Nevertheless, direct comparison of the 2 studies is not the main intent of this paper and is probably not meaningful as real changes in population HRQoL may have occurred over the 5 years since the previous study was conducted. Furthermore, the SF-36v2 has now superseded the SF-36v1.

Conclusion

In this paper, we have provided detailed normative data for

users of the English (Singapore) and Chinese (Singapore) SF-36v2, which would be valuable in furthering research in HRQoL in Singapore and possibly the region, particularly in countries without population reference values.

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Surgical Outcome in Thoracolumbar Fractures Managed by Short-segment Pedicle Instrumentation

Min Yang,^{1MD, PhD}, Guo Zheng Ding,^{1MD}, Zhu Jun Xu,^{1MD}

Abstract

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Key words: Short-segment fixation, Spine, Kyphosis angle

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Introduction

Thoracolumbar junction vertebrae are particularly vulnerable in traumatic injuries and up to 90% of all spinal fractures occur in this area.¹ Treatment of thoracolumbar fractures has been a controversial subject for many years.²⁻⁴ Non-operative management recommended by some authors is effective when there is no evidence of neural compression or spinal instability. However, operative intervention should be seriously considered when a fracture is complicated by progressive neurological deficiency or in situations like neural element compression, fracture dislocation or progressive symptomatic kyphosis.^{5,6} The goals of surgical treatment of thoracolumbar fractures are to restore vertebral column stability, decompress the neural tissue, facilitate

neurological recovery, and prevent loss of correction with neurological impairment.^{4,6} Different surgical strategies and treatment methodologies were developed in past decades, but no one single method is clearly better than the rest, making it difficult to determine the optimal treatment strategy.⁷⁻⁹ Orthopaedic surgeons should consider the efficiency and advantages of different fracture segment fixation approaches (anterior, posterior), fixation ranges (short-, intermediate- or long-segment fixation), and whether or not bone grafting is necessary. An anterior approach can provide excellent visualisation for decompression of neural elements and easy access for reconstruction of the anterior column with a load-sharing construct. However, an anterior

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approach may be more technically demanding for obtaining a clear exposure, and thorough neural decompression, which can increase morbidity and potential vascular injuries.^{2,4} On the other hand, a posterior approach is technically less challenging. As a result, this approach is recommended by majority of the spinal surgeons as the choice of treatment for unstable thoracolumbar injuries.

Pedicle screw devices allow immediate stable fixation since the screws traverse all the 3 columns. Advances in spinal instrumentation have led to the development of short-segment spinal instrumentation which provides sufficient fixation power without the need to fuse uninjured motion segments. Ever since Dick et al¹⁰ introduced this technique, short-segment pedicle instrumentation has become a popular method for treating thoracolumbar vertebral fractures.¹¹ As a result, fewer motion segments are incorporated, and postoperative morbidity is decreased. Like any other methods, this method has been associated with some complications such as early implant failure of fixation with progressive kyphosis. When treating unstable thoracolumbar fractures, different types of instrumentation for fixation have been described in practice such as “2 levels above and 1 level below pedicle screw fixation” and “1 level above and 1 level below including the fracture level pedicle screw fixation”.^{9,12-14}

To ensure proper use of short-segment spinal instrumentation and prevent any possible failure of fixation, McCormack et al¹⁵ who introduced a Load Sharing scoring system concluded that thoracolumbar fractures with a score of 7 points or more would ultimately result in a short-segment implant failure. Earlier studies reported the suboptimal outcomes with short-segment fixation based on this scoring system. Recent studies, however, demonstrated favourable clinical results compared to studies in the past.^{7,16-21} In our institute, short-segment fixation has been the choice of treatment for thoracolumbar fracture since 2007. Excellent spinal reduction, decompression of the neural elements, and spinal reconstruction were observed in all patients treated with this method, without any failed cases. This retrospective study evaluated the radiological and clinical outcomes from short-segment fixation in 22 patients. The Load Sharing scores alone might not be reliable in predicting posterior instrumentation failure as thoracolumbar fractures patients with high Load Sharing scores could still be successfully treated by short-segment fixation in our institute.

Materials and Methods

Study Patients

Posterior short-segment pedicle instrumentation was performed in 22 patients including 13 males and 9 females between 2007 and 2010. Patients' mean age was 38 ± 17

years. Causes of injury included motor vehicle accidents (8 patients), falling from a height (12 patients) and unspecified causes (2 patients). The average postoperative follow-up period lasted 15 ± 3 months.

Case Selection

Indication for the need for short-segment pedicle fixation included at least one of the following:^{4,7} posterior ligamentous complex failure, neurological injury, kyphosis of more than 20° as shown by radiographic imaging, loss of more than 50% vertebral body's height, compromised spinal canals, and spinal instability (based on the criteria of unstable thoracolumbar fractures by McAfee et al²²). Patients with osteoporosis or low bone mineral density (BMD) were at high risk of pedicle screw pullout.⁷ BMD was measured in all patients preoperatively, and patients aged over 55 years or had a BMD < -2.5 standard deviations (SD) below the young adult reference range were excluded for the short-segment intervention.

Radiographic Measurements

Plain radiographs were obtained at preoperative, immediate postoperative, and final follow-up (average duration of 15 months). Initial supine X-rays were taken because of the acuteness of the injury. Upright radiographs were obtained at the follow-up evaluations. For each lateral X-ray film, the following parameters were manually measured by 2 independent examiners according to the method described by Kim et al³ (Fig. 1). Regional kyphosis angle (RA) was defined as the angle between the superior endplate of the superior adjacent vertebra and the inferior endplate of the inferior adjacent vertebra.



Fig.1 Schematic diagram of regional kyphosis (RA) and anterior body height compression (AVC) using the method of Kim et al.³
RA = angle between c and d; AVC = $2e/(f+g) \times 100$

Anterior vertebral body compression percentage (AVC) was calculated as the anterior height of the injured vertebra divided by average height of 2 adjacent anterior vertebrae. The sagittal index (SI) was the local kyphosis at a motion segment minus the baseline sagittal curve at the level of fracture according to the method of Farcy et al.²³ Possible vertebral body comminution and canal encroachment by bone fragments from the fractured vertebra were assessed by computed tomographic (CT) scan upon admission. The greatest narrowing of the spinal canal at the level of the fractured vertebra was measured, and compared with the average measurements of the vertebrae above and below. After the surgery, all patients received a CT scan to assess spinal canal restoration, and to determine the preoperative to postoperative canal compromise ratio. All fractures were classified using the AO classification of fractures system. The spinal injuries were also evaluated according to the Load Sharing spine fracture system scores outlined by McCormack et al.¹⁵

Surgical Techniques

Patients were carefully logrolled into a hyper extended, prone position with the abdomen hanging free for the purpose of minimising bleeding from the epidural venous plexus and achieving a significant initial reduction of the spinal fracture. All patients underwent short-segment posterior titanium alloy pedicle screw fixation, including 1 level above and 1 level below the fractured vertebra. For cases of highly comminuted fractures, screw fixation covered vertebrae “2 above and 1 below” the comminuted 1 (Fig. 2) or “inclusion of the fracture level” (Fig. 3). Pedicle screw constructs were used. The intermediate screws were used at the fracture level in all except 3 of the patients with comminuted fractures of the pedicle. The polyaxial screws were only placed at the fractured vertebra, with monoaxial screws placed at adjacent levels. After pedicle screw instrumentation, the 6 mm rods were contoured to reproduce the normal sagittal curvature of the thoracolumbar spine. The rods were then

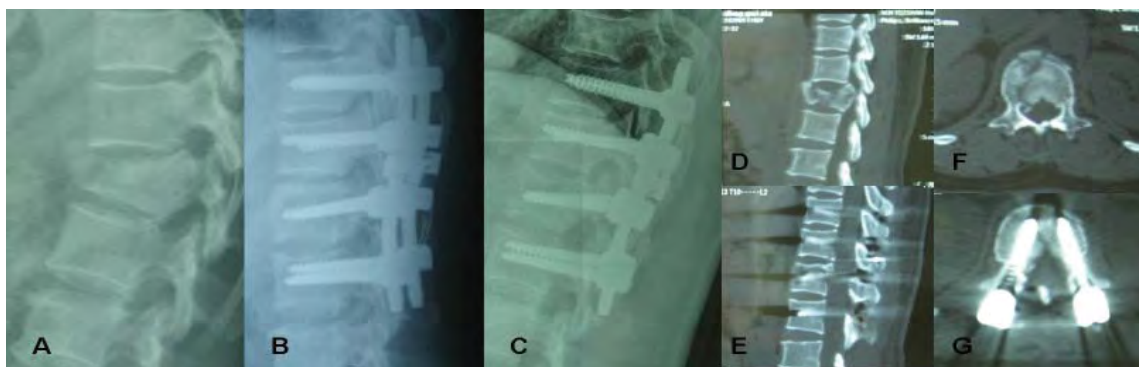


Fig.2. Images of L1 unstable burst fracture in a 46-year-old female who fell from a height. (A) Preoperative lateral plain radiograph; (B) Lateral view of immediate postoperative result: two above-one below instrumentation with intermediate screws at the fracture level. (C) Radiograph at 15 months post-operation showed good maintenance of correction. (D,F) Preoperative CT scan images in axial and sagittal planes revealed a spinal canal compromise of about 45%; (E,G) Postoperative CT scan images in axial and sagittal planes revealing a reduction of spinal canal occupation and the intermediate screws at the level of the fracture.

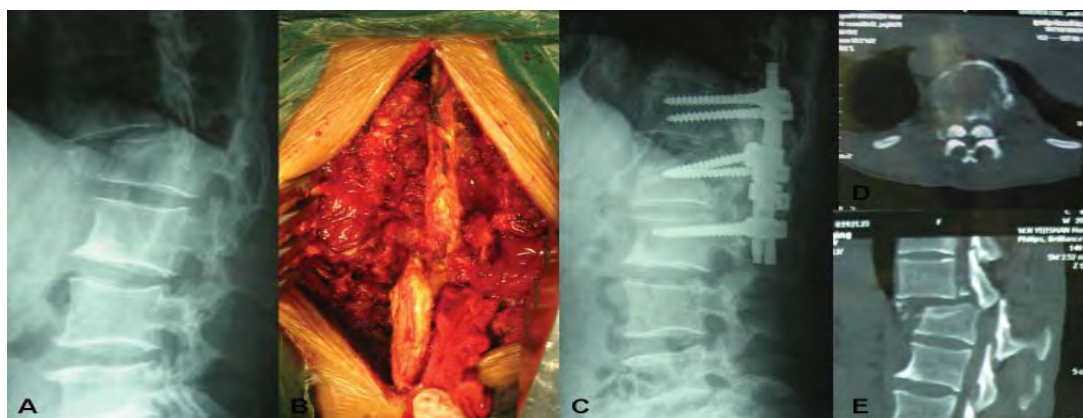


Fig.3. Images of L1 unstable burst fracture in a 54-year-old male who fell from a height. (A) Preoperative lateral plain radiographs. (B) Intraoperative photo showing the posterior ligamentous disruption. (C) Postoperative lateral X-ray showed the optimal correction of kyphosis and realignment by the short-segment instrumentation with intermediate screws at the fracture level; (D, E) Preoperative CT scan images in axial and sagittal planes revealing severe spinal canal compromise and fracture-dislocation.

fixed within the heads of the pedicle screws, and torque was applied through the rod pusher to bring the vertebra back to the rod. Reduction of the fracture was accomplished by applying a gentle distraction force at the level of the fracture (ligamentotaxis).² Decompression, by total or partial posterior laminectomy, was performed only in cases where the spinal canal was narrowed by more than 50% by free bone fragments. This was followed by pushing back those bone fragments into their original positions (Fig. 4). A cross connector was used to link the rods. Either an interlaminar or an intertransverse process type of posterior fusion was performed by the authors. All patients were required to wear a rigid thoracolumbar orthosis (TLSO) for a minimum of 3 months postoperatively when they were able to stand upright. In this study, all implants were removed at an average time of 15 months after the surgery.

Clinical Assessments

Patients' preoperative neurological status and endpoint follow-up status after the surgery were recorded according to the modified Frankel's classification.²⁴ Denis' Pain and Work scales²⁵ were used to evaluate the clinical outcomes.

Statistical Analysis

Statistical analysis was carried out using SPSS13.0. Comparisons were performed using the Student's *t*-test for continuous data (changes in radiographic parameters over time), or for the average loss of correction in patients with Load Sharing score of ≤ 6 and ≥ 7 . The ANOVA test was carried out to compare the average loss of correction measured in AO type of A, B, and C. The probability level was set at $P < 0.05$.

Results

Radiographic Results

The average SI was 19.1° preoperatively, 3.1° immediate postoperatively, and 4.6° at the final follow-up with a correction loss of 1.5°. Each group's SI was significant different ($P = 0.02$). The mean AVC was 40.8% preoperatively, 90.2% immediate postoperatively, and 88.2% at the final follow-up with loss of body height of 2.0% in average. Each group's value was significantly different ($P = 0.01$). The average RA was 21° preoperatively, 3.5° postoperatively, and 5.6° at the final follow-up with a correction loss of 1.1°. This difference of value was also statistically significant ($P = 0.01$) (Table 1).

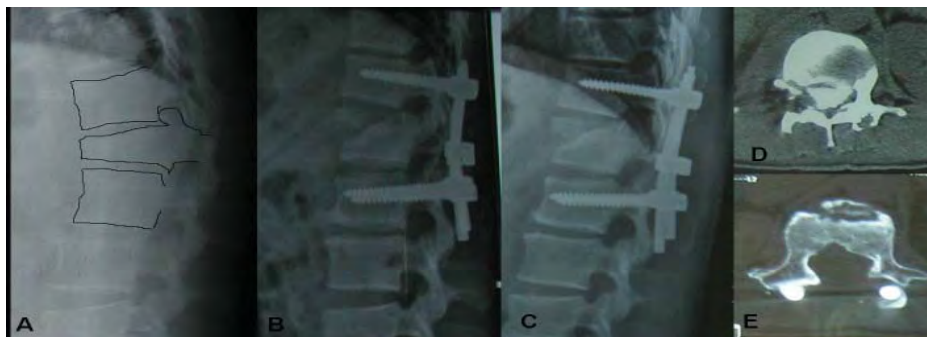


Fig. 4. Images of L1 unstable burst fracture in a 54-year-old male injured in a motorcycle accident. (A) Preoperative lateral plain radiograph. (B) Good correction achieved in the immediate postoperative lateral radiogram. (C) Good correction maintained at the final follow-up (15 months). (D) Preoperative CT scan in axial showed the spinal canal being completely narrowed by a retropulsed bony fragment. (E) Last follow-up axial CT image showed excellent remodeling in canal compromise.

Table 1. Changes in Radiographic Parameters over Time (Mean $\pm$ Standard Deviation)

Parameter	Preop	Postop	At final follow-up	Loss of correction	<i>P</i> values
RA (°)	21 $\pm$ 5.2	3.5 $\pm$ 6.5	5.6 $\pm$ 5.9	1.1 $\pm$ 0.9	0.01
SI (°)	19.1 $\pm$ 4.8	3.1 $\pm$ 5.4	4.1 $\pm$ 6.0	1.5 $\pm$ 2.1	0.02
AVC (%)	40.8 $\pm$ 12.5	90.2 $\pm$ 14.7	88.2 $\pm$ 13.8	2.0 $\pm$ 4.6	0.01

RA: Regional kyphosis angle; SI: Sagittal index; AVC: Anterior vertebral body compression percentage

According to AO classification of fractures system, these 22 cases were classified into 3 types: 13 cases were type A, 5 were type B and 4 cases were type C respectively. In type A fractures, the average RA values preoperatively, postoperatively, and at final follow-up were 19°, 3.0° and 4.1° respectively, with a loss of correction averaging 1.1°. In type B fractures, the respective values were 22°, 3.4° and 4.6°, with a loss of correction averaging 1.2°. In type C fractures, the respective values were 21°, 5.25° and 7°, with a loss of correction averaging 1.75°. There were no significant differences in RA values among the 3 groups according to AO classification (Table 2).

Sixteen patients had their Load Sharing scores ≤ 6 . The respective average RA preoperatively, postoperatively, and at final follow-up were 20.1°, 3.3° and 5.2° with a loss of correction averaging 1.9°. On the other hand, analysis of patients with Load Sharing scores ≥ 7 showed the respective

average RA values as 23.6°, 4.1° and 6.6° with a loss of correction averaging 2.5°. There were no significant differences in RA values between the 2 groups according to the Load Sharing scoring system (Table 3).

The cross-sectional area of the spinal canal was narrowed initially by an average of 45%. After the surgery, the narrowing was reduced to an average value of 6.7%. All the patients experienced significant improvement in spinal canal cross-section after the operative reduction by pushing back retropulsed bony fragments into their original positions.

Clinical Outcomes

At the final follow-up, back pain and movement disability were reduced significantly in 21 patients (95%), with the majority of patients reporting slight or no pain. These patients showed complete recovery and were able to resume their daily activities. (Table 4)

Table 2. Changes in Regional Kyphosis Angle According to AO classification (Mean $\pm$ Standard Deviation)

AO type	Preop (°)	Postop (°)	At final follow-up (°)	Loss of correction (°)
A (n = 13)	19 $\pm$ 4.7	3.0 $\pm$ 5.8	4.1 $\pm$ 5.1	1.1 $\pm$ 2.3
B (n = 5)	22 $\pm$ 5.3	3.4 $\pm$ 4.8	4.6 $\pm$ 4.3	1.2 $\pm$ 1.7
C (n = 4)	21 $\pm$ 4.2	5.25 $\pm$ 5.0	7.0 $\pm$ 5.8	1.75 $\pm$ 2.6
P value	0.37	0.13	0.08	0.61

Table 3. Changes in Regional Kyphosis Angle According to Load Sharing Score (Mean $\pm$ Standard Deviation)

Load Sharing score	Preop (°)	Postop (°)	At final follow-up (°)	Loss of correction (°)
≤ 6 (n = 16)	20.1	3.3	5.2	1.9
≥ 7 (n = 6)	23.6	4.1	6.6	2.5
P value	0.07	0.33	0.12	0.36

Table 4. Distribution of Patients Classified According to the Denis et al's Pain and Work Scale

Pain scale grade	No. of Patients	Work scale	No. of Patients
1. No pain	14	1. Heavy labor	15
2. Occasional, minimal pain	6	2. Sedentary job or lift restrictions	5
3. Moderate pain, no work interruption	1	3. Unable to return to previous work, but working full time	1
4. Moderate to severe pain, absence from work	1	4. Unable return to full time job	0
5. Constant severe pain, incapacitation	0	5. Unable to work	1

Table 5. Preoperative and Final Follow-up Neurological Status of 22 Patients

Preoperative neurological status	No. of Patients	Final follow-up neurological status				
		A	B	C	D	E
A	0	0	0	0	0	0
B	2	0	1	0	1	0
C	5	0	0	0	1	4
D	8	0	0	0	1	7
E	7	0	0	0	0	7

Neurological Recovery

There was no neurological deterioration as a result of the operative treatment. According to the Frankel grading system, 21 of 22 patients (95%) with incomplete injuries showed improvement by at least one grade (range, 1 to 2 grades). As an example, for immediate grade C postoperation, 4 cases improved to grade E at final check-up, and 1 case to grade D. There were 2 cases, 1 of grade B and 1 of grade D, where neither improvement nor deterioration were observed (Table 5).

Complications

There were no cases of implant failure due to pedicle screw breakage, loosening or disengagement. There were also no thrombophlebitis and superficial or deep wound infection. One patient with urinary tract infection was successfully treated with antibiotics.

Discussion

The concept of posterior transpedicular fixation of the spine was first introduced in the mid 1950s by Dr Roy-Camille²⁶ who used pedicle screw plates for the stabilisation of spinal injuries. Transpedicular screw fixation offers superior 3-column control and obviates the need for intracanal placement of hardware. Presently, the pedicle screw system represents a gold standard of spinal internal fixation.⁴ Short-segment posterior fixation is the most commonly used and has the advantage of incorporating fewer motion segments in the fusion, thus causing less morbidity than other methods. Although considered as a gold standard for treatment of thoracolumbar fractures, clinical outcomes reported about using short-segment pedicle is not consistent, which include a 5% to 94% failure rate of implants presumably due to several factors including implant failure, recurrent kyphosis and moderate-to-severe pain.^{3,27-29} Therefore, this method of fixation needs to be carefully re-evaluated. Our study provides an opportunity to re-examine the clinical outcomes when modern instrumentation and techniques are used during short-segment pedicle fixation.

To better predict the high failure rate of this method, McCormack et al¹⁵ advanced a classification system based on the Load sharing score. Three main factors are considered in this scoring system: the extent of the entire vertebral body comminution, the quantification of displacement for bony fracture fragments, and the amount of kyphosis correction necessary to restore the physiologically normal sagittal plane alignment at the level of the injury. Using this scoring system, Parker et al¹⁹ reported that short-segment instrumentation successfully treated thoracolumbar fractures when the load sharing score was 6 points or less, while those patients with scores over 7 points were treated with alternative surgery by anterior short-segment fixation to support the anterior column. As mentioned above, the risk of an anterior approach was higher than posterior approaches, and single anterior fusion might fail in cases with disrupted posterior stabilising elements. Meanwhile, long-segment fixation (bridging 2 to 3 levels above and 2 levels below the fractured vertebra) to lengthen the level arm of the construct were reported^{30,31} to enhance spinal stability and allow effective reduction of kyphotic deformity. However, long segment fixation could also result in stiffness and discomfort, and, it could not preserve the motion segments. Therefore, it was not suitable for treating young patients.^{3,9}

Differ from the literature, Gelb et al¹⁶ recently conducted a retrospective study of 27 patients with thoracolumbar fractures operated upon with short-segment fixation regardless of fracture pattern, injury level, associated injuries, or load sharing classification. The average length of follow-up was 14.4 months. They found no correlation between (i) loss of correction and load sharing classification, (ii) loss of correction and AO classification, (iii) or loss of correction and level of injury. None of the 27 patients experienced implant failure in terms of pedicle screw breakage, bending, loosening or pull-out. This study concludes that short-segment fixation without postoperative bracing could be successful in the treatment of thoracolumbar fractures. Short-segment fixation has been the choice of treatment for thoracolumbar fractures in our institute since 2007, and similar favourable clinical

outcomes were obtained as in Gelb et al.¹⁶ We believe that our success in using short-segment instrumentation is attributed to the following:

1. Strict exclusion criteria were set. To avoid implant failure, patients aged 55 years and above or with a BMD <2.5 SD below the young adult reference range were not treated with short-segment instrumentation. As a result, no cases of pedicle screws pull-out and loss of correction due to osteoporosis were found in this study. Although the pedicle screws could provide 3-column fixation, screw loosening has often been reported in elderly patients, probably due to poor bone quality which decreased the strength of pedicle screw fixation.^{7,9,18,20,32}
2. In studies by Lee²⁰ and Kim²¹, there were 3 failure cases due to osteoporosis. Thus, we would always consider alternative techniques such as long-segment fixation when treating the patients. In general, methods that avoid ending instrumentation within the kyphotic segment should be considered^{21,32} instead of short-segment instrumentation for fractures complicated by osteoporosis. We chose not to remove any comminuted bony fragments. Instead, they were pushed back into their original positions, hence restoring the anterior and mid-column stability to prevent future increases in kyphotic deformity after obtaining an initial correction. The posterior approach is a method familiar to most of the spinal surgeons. During the surgery, a small impactor was used to push the comminuted bony fragments into their original position in patients undergoing total or partial laminectomy by the posterior approach. As a result of this action, we had adequate spinal canal decompression with an average canal narrowing reduction from 45% to 6.7% and satisfactory neurological recovery in 21 cases. In the recent study by Jun et al,¹⁷ the surgeons did not perform impaction of large bony fragments, but opted to remove them to achieve adequate decompression for fear that the impacted bony fragments might displace and compress the nerves in some of the patients. However, we believe that the removal of the bony fragments is not suitable for the patients with thoracolumbar fractures. First, without the support of the anterior and mid-column, recurrent kyphosis and instrumentation failure had been observed frequently after posterior short-segment pedicle fixation for a thoracolumbar fracture.^{1,4,33} In this study, we impacted the displaced bony fragments into the original positions to reconstruct the anterior and mid-column, and used this bony fragment as a strut graft to restore the anterior and mid-column stability, and to prevent

future increased kyphotic deformity after obtaining an initial correction. Second, some authors^{8,34} have described spontaneous remodelling of the spinal canal during the follow-up period. We found no cases with impacted bony fragment displacement and nerve recompression in this study. Although the relation between the canal diameter and its association with neurological sequelae after trauma remains unclear, this study shows that the neurological improvement is associated with a remarkable clearance of the spinal canal.

3. With advance medical instrumentation and good surgical techniques, posterior short-segment fixation provides satisfactory clinical outcomes. The currently used posterior pedicle system allows a link between a pedicle screw and a rod of optimal diameter. The link is constructed by a connecting element that can change the inclination between the screw and the rod axes in vertical and horizontal planes. The system is completed by a threaded locking mechanism that firmly locks the connecting element rotation, and subsequently allows the surgeon to fix the rod inclination in the most suitable position. Therefore, this special screw-to-rod locking mechanism undoubtedly has contributed to the reduction of instrumentation failure.¹⁶ At the same time, several authors demonstrated that intraoperative rod contouring and corrective procedures using reduction devices were generally thought to be risk factors for the failure of spinal constructs, particularly with pure titanium or titanium alloy implants due to their notch sensitivity.³⁵⁻³⁷ We precontoured the rod and used a cantilever-type method to introduce the rod into the screws without performing any in situ bending of the rod. We thought the precontoured rod would likely provide a 3-point bending force as the apex of the rod would engage the intermediate injured vertebra. The technique of including pedicle fixation at the fracture level into a posterior construct has offered a better kyphosis correction and a stronger 3-point posterior support to reduce instrument failures. In a cadaveric biomechanical study by Mahar et al,¹⁴ it was demonstrated that insertion of the pedicle screws at the fracture level could strengthen the construct biomechanically. As seen in the results of this study, there was a variable amount of postoperative loss of correction at the last follow-up while there were no patients with more than 10° correction loss in the sagittal plane, and correction of the kyphotic deformity was well-maintained. We attributed the correction loss primarily to disc space collapse, and it seemed that the final clinical outcomes (pain and

work scale) had no relation with the correction loss, which was limited to 10°.

Finally, some studies have suggested that the Load sharing scoring system was a reliable and easy-to-use classification scheme for choosing the treatment method for thoracolumbar fractures.^{19,38} By using this scoring system, Parker et al¹⁹ predicted that fractures with a score 6 or less could be safely treated with short-segment posterior fixation with low risk of implant failure or progressive deformity. However, an anterior strut graft with longer instrumentation should be used to treat the fractures with a score of 7 or more.

In our institute, all the patients who met inclusion criteria, whether the Load Sharing score point ≤ 6 or ≥ 7 , were operated upon with posterior short-segment fixation. There were no cases of implant failure in terms of pedicle screws breakage, loosening or disengagement. Therefore, we found that it was not necessary to emphasise that the fractures with a Load Sharing score ≥ 7 needed an anterior-only approach, or a staged anterior reconstruction or augmentation following a posterior approach.

In a similar study, Farrokhi et al,¹³ concluded that fracture level pedicle screw combination could achieve and maintain kyphosis correction, and there were no evidence to emphasise that fractures with Load Sharing scores of 7 or more should be treated by an anterior approach. Nevertheless, there are some differences in the results based on Load Sharing scores, although they do not affect the overall clinical outcome. We found that patients with a Load Sharing score ≥ 7 had an average of 2.5° loss of correction, compared with a 1.9° loss of correction in patients with a point ≤ 6 at the final follow-up ($P > 0.05$).

Limitations

This study has several limitations. First, it was a retrospective design with a small number of patients and short-term follow-up. Second, it was not a randomised control study as there were no controls to compare the outcomes. Thus, it was not a comparative study between the posterior long-segment fixation and anterior approach fixation. Finally, we could not evaluate the effects of bone fusion on the final outcome in all the patients because not all subjects underwent CT scan at the final follow-up. We hope to conduct a larger scale prospective randomised study to confirm our findings and address the above issues in the near future.

Conclusion

With advanced medical instrumentation and good surgical techniques, the results from this study favour a posterior approach with short-segment fixation for thoracolumbar fracture patients younger than 55 years old and are free

of osteoporosis, even though the fracture is classified as highly comminuted fracture.

Acknowledgements

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Effect of Using an Audiovisual CPR Feedback Device on Chest Compression Rate and Depth

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Abstract

Introduction: The aim of the study is to investigate the effect of using Automated External Defibrillator (AED) audiovisual feedback on the quality of cardiopulmonary resuscitation (CPR) in a manikin training setting. **Materials and Methods:** Five cycles of 30 chest compressions were performed on a manikin without CPR prompts. After an interval of at least 5 minutes, the participants performed another 5 cycles with the use of real time audiovisual feedback via the ZOLL E-Series defibrillator. Performance data were obtained and analysed. **Results:** A total of 209 dialysis centre staff participated in the study. Using a feedback system resulted in a statistically significant improvement from 39.57% to 46.94% ($P = 0.009$) of the participants being within the target compression depth of 4 cm to 5 cm and a reduction in those below target from 16.45% to 11.05% ($P = 0.004$). The use of feedback also produced a significant improvement in achieving the target for rate of chest compression (90 to 110 compressions per minute) from 41.27% to 53.49%; ($P < 0.001$). The mean depth of chest compressions was 4.85 cm (SD = 0.79) without audiovisual feedback and 4.91 (SD = 0.69) with feedback. For rate of chest compressions, it was 104.89 (SD = 13.74) vs 101.65 (SD = 10.21) respectively. The mean depth of chest compression was less in males than in females (4.61 cm vs 4.93 cm, $P = 0.011$), and this trend was reversed with the use of feedback. **Conclusion:** In conclusion, the use of feedback devices helps to improve the quality of CPR during training. However more studies involving cardiac arrest patients requiring CPR need to be done to determine if these devices improve survival.

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Key words: Cardiopulmonary resuscitation, Chest compression, Quality

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Effect of Using an Audiovisual CPR Feedback Device on Chest Compression Rate and Depth

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Introduction

There is increasing evidence to show that good quality cardiopulmonary resuscitation (CPR) is important in achieving better resuscitative outcomes.^{1,2} One of the determinants for successful defibrillation is the effectiveness of chest compressions.

The 2005 International Liaison Committee on Resuscitation (ILCOR) guidelines for CPR and Emergency Cardiovascular Care (ECC) recognised the importance of early CPR with an emphasis on chest compressions. The guidelines recommended providing high quality CPR that included chest compressions at an adequate rate (of about 100 per minute), with adequate depth (4 cm to 5 cm) while allowing complete chest recoil. There should be minimal

interruptions to compressions while avoiding excessive ventilation.³ ILCOR has published a set of guidelines in 2010 which recommended a chest compression depth of least 2 inches (5 cm) and at a rate of at least 100 compressions per minute, allowing full chest recoil after each compression, and minimising interruptions in chest compressions.³ Some studies show that the quality of CPR being performed both in-hospital and out-of-hospital is suboptimal.^{4,5} This further highlights the importance of CPR training and constant practice.

A number of audiovisual feedback devices have been designed to improve the quality of CPR and resuscitation outcomes.^{6,7} These vary from being a beeping timer to more complex devices. Data can be obtained from some

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of these devices and can be used in further training and to achieve a higher standard of CPR. A systemic review done by Yeung et al⁷ showed good evidence supporting the use of CPR feedback/prompt devices during CPR training to improve CPR skill acquisition and retention.

Haemodialysis patients have an incidence of cardiac related death 10 to 20 times higher than that of the general population. In the United States, Karnik et al⁸ showed a frequency of 7 cardiac arrests per 100,000 haemodialysis sessions, with ventricular tachycardia/fibrillation being the predominant abnormal recorded rhythm. In Singapore, from October 2001 to September 2004, there were 19 out-of-hospital cardiac arrests (OHCA) occurring in dialysis centres.⁹ Only 2 of these patients survived.

As part of this study, we introduced Automated External Defibrillators (AEDs) to all National Kidney Foundation (NKF) dialysis centres in Singapore, as well as a programme to train all NKF staff in CPR and AED skills. This would allow their nursing staff first responders to give life-saving defibrillation in the event of a cardiac arrest, even in the absence of a doctor. This upgrading of defibrillators was in parallel to the training of staff described in this study.

The aim of this observational prospective manikin study is to investigate if the use of an AED audiovisual feedback device could objectively improve the quality of CPR in a manikin training setting.

Materials and Methods

Setting

An observational prospective manikin study was conducted to look at the effect of introducing an audiovisual feedback device for NKF staff on the quality of CPR.

The NKF is a registered charity and is Singapore's largest provider of outpatient dialysis services and rehabilitative care to patients with renal failure at affordable rates. Its 24 dialysis centres are staffed by health care personnel (registered/enrolled nurses, healthcare assistants) who are trained in provision of dialysis services. Before this study, staff were only equipped with manual defibrillators which require the presence of a doctor for operation. This meant that in most cases, attending first responders were not able to give life-saving defibrillations as doctors are not usually present in the dialysis centres. The quality of CPR being performed was also unknown. In the previously mentioned study, none of the cardiac arrests that occurred in dialysis centres received pre-ambulance defibrillation.⁹

Participants

Participants involved were from 14 of the 24 NKF dialysis centres. Between January 2010 and December 2010, a study

coordinator travelled to these 14 dialysis centres to perform data collection. Participants also filled out an anonymous survey form with included information on demographics; knowledge and attitude towards CPR and AED.

Data Collection

During data collection, a training manikin (AmbuMan manikin, Ambu; Copenhagen, Denmark) was used. A defibrillator with an accelerometer (ZOLL E Series; ZOLL Medical, Chelmsford, MA) was used for measuring of compression rate (chest compression/min [cpm]) and compression depth (cm). Data were recorded via the defibrillator, which has a real-time audiovisual feedback prompt, and Code Review software (ZOLL Data Systems, Broomfield, CO) was used to analyse the collected data. Data variables collected were compression rate and compression depth.

The participants performed 5 cycles of 30 chest compressions on a training manikin placed on firm, flat ground without feedback prompts. Subsequently, after a break of at least 5 minutes the participants were orientated on the real-time audiovisual feedback feature in the defibrillator. Participants were then instructed to perform another 5 cycles of 30 chest compressions on the same manikin with the use of real time audiovisual feedback prompts.

A chest compression rate of 90 to 110 compressions per minute and a chest compression depth of 4 cm to 5 cm was considered to be in compliance with the ILCOR 2005 guidelines.³ Compliance to the ILCOR 2010 guidelines was not assessed as that was not yet adopted in the centers studied.

Statistics

Statistical analysis was performed using SPSS 18.0 with statistical significance set at $P < 0.05$. Basic descriptives for numerical data were presented as mean (SD) and n (%) for categorical data. The comparison on depth and rate of compression before and after feedback were analysed using paired t-test if normality assumptions were satisfied. Otherwise the non-parametric Wilcoxon Signed rank test was used. McNemar's test was performed to assess the efficacy of feedback against no-feedback on the categorical depth and compression rate targets. Differences between gender on the compression rate and depth were analysed using 2 Sample t-test if normality and homogeneity assumptions were satisfied. Otherwise the Mann Whitney test was performed. A general linear model was performed to determine the predictors for depth and rate compression subgrouped by with and without feedback.

Results

A total of 209 NKF personnel were approached to participate in this study with a participation rate of 100%. Most of the participants fell between 20 and 39 years of age and were female (75%). The majority had at least a nursing Diploma and held a valid Basic Cardiac Life Support (BCLS) and AED certificate. In the study group, most had not attended to any cardiac arrest patients previously (Table 1).

Table 1. Characteristics of Study Participants

Characteristics	n = 209 (%)
Mean Age (SD)	32.9 (8.0)
Age Group (years)	
20 – 29	85 (40.7)
30 – 39	88 (42.1)
40 – 49	28 (13.4)
≥ 50	8 (3.8)
Gender	
Male	51 (24.4)
Female	158 (75.6)
Profession	
Registered Nurse	122 (58.4)
Enrolled Nurse	62 (29.7)
Health care assistant/ Patient care assistant	17 (8.1)
Patient care technician/ Senior patient care technician	3 (1.4)
Others	5 (2.4)
Qualification (n = 205)	
Diploma	70 (34.1)
Advance Diploma	20 (9.8)
Degree	99 (48.3)
NITEC	12 (5.9)
Others	4 (2.0)
Basic Cardiac Life Support	
Trained	188 (90.0)
Valid Certificate	174 (83.3)
Automated External Defibrillation	
Trained	177 (84.7)
Valid Certificate	177 (84.7)
Attended to cardiac arrest cases	29 (13.9)
No. of cardiac arrest cases attended to (%) (n = 29)	
1	20 (69.0)
2	6 (20.7)
Unknown	3 (10.3)

Without audiovisual feedback, the overall mean depth of chest compressions was 4.85 cm (SD = 0.79) and rate of chest compressions was 104.89 (SD = 13.74). With the use of audiovisual feedback, the overall mean depth of chest compressions was 4.91 (SD = 0.69) and mean rate of chest compressions was 101.65 (SD = 10.21). There was a statistically significant difference in the overall mean compression rate with the use of feedback compared to without (Table 2).

When chest compressions were performed without feedback, only 39.57% of the participants were in compliance with the 2005 ILCOR guidelines for compression depth. When feedback was available, there was a statistically significant improvement to 46.94% ($P = 0.009$) of the participants being within the target depth. Of note, there was a statistically significant decrease in the number of participants below the target depth. The use of feedback also produced a statistically significant improvement in achieving the target for the rate of chest compression (from 41.27% to 53.49%; $P < 0.001$). (Table 3)

There was no statistical difference between male and female participants in mean compression rate without feedback ($P = 0.788$). With feedback there seemed to be a greater difference, which was statistically significant ($P = 0.069$). Interestingly, the mean depth of chest compression was less in males than in females and this trend was reversed with the use of feedback. Without feedback, the male participants had a significantly lower compression depth as compared to females ($P = 0.011$); with feedback there was no statistically significant difference (Table 4).

There was no statistically significant difference in mean chest compression rates and depth with and without feedback among groups with different qualifications, training and age. Although there was a statistically significant difference in the mean compression rates with and without feedback between groups with different qualifications, that is unlikely to be clinically significant (Table 5).

Discussion

In this study, we found that with audiovisual feedback, there was a statistically significant improvement from 39.57% to 46.94% ($P = 0.009$) of the participants being within the target compression depth of 4 cm to 5 cm and a reduction in those below target from 16.45% to 11.05% ($P = 0.004$). The use of feedback also resulted in a statistically significant improvement in achieving the target for the rate of chest compression (90 to 110 compressions per minute) from 41.27% to 53.49% ($P < 0.001$).

Recent research indicates that the quality of CPR is an important factor in affecting survival^{10,11} and the ILCOR Advanced Cardiac Life Support Guidelines 2005 suggest

Table 2. Comparison of Depth and Rate of Compressions with and Without Feedback

	Without Feedback	With Feedback	Mean difference	95% Confidence interval	P value
Mean Depth (cm) (SD)	4.85 (0.79)	4.91 (0.69)	– 0.06	– 0.06 to 0.05	0.280
Mean Rate (cpm) (SD)	104.89 (13.74)	101.65 (10.21)	3.24	1.57 to 4.91	<0.001

Table 3. Comparison of Compression Depth and Rate with and Without Feedback

	Without Feedback (%)	With Feedback (%)	Difference	95% Confidence interval	P value
Depth					
Below target	16.45	11.05	5.41	1.76 to 9.05	0.004
In target	39.57	46.94	– 7.37	– 12.90 to – 1.84	0.009
Above target	43.98	42.02	1.96	– 4.17 to 8.08	0.530
Rate					
Below target	15.16	15.55	– 0.39	– 3.96 to 3.18	0.829
In target	41.27	53.49	– 12.22	– 17.63 to – 6.80	<0.001
Above target	43.56	30.96	12.61	7.41 to 17.80	<0.001

Table 4. Mean Compression Depth and Rate Between Different Genders

	Without feedback (SD)	95% Confidence interval	With feedback (SD)	95% Confidence interval
Mean Depth				
Male	4.61 (0.91)	4.36 – 4.86	4.92 (0.71)	4.72 – 5.13
Female	4.93 (0.73)	4.82 – 5.05	4.90 (0.68)	4.80 – 5.01
Mean Rate				
Male	105.34 (14.08)	101.38 – 109.30	99.38 (12.37)	95.90 – 102.87
Female	104.74 (13.67)	102.59 – 106.89	102.38 (9.34)	100.91 – 103.85

that good quality CPR can be as important as the presence of bystander CPR.¹² Insufficient depth of chest compressions is associated with poorer outcome from cardiac arrest.¹³ It is shown that the use of audiovisual feedback devices can improve the quality of CPR where chest compression depth and rate are concerned, and these devices can be used as part of training and during actual CPR during a real cardiac arrest scenario. Furthermore, if the quality of CPR is deteriorating, it may be a sign of fatigue and the person performing CPR should be swapped. Rescuer fatigue has been shown to adversely affect the quality of CPR.¹⁴ Perberdy et al¹⁵ showed improvements with the use of a similar accelerometer based audiovisual feedback device and had concluded that these devices can be used to improve the quality of CPR.

In contrast to these studies, we found that there was no statistically significant difference in chest compression rates and depth when groups of different gender, age, profession and training were compared. This could mean that the proficiency or ability of the participants to meet the ILCOR guideline targets are not significantly affected by

any of the above variables, and that most can adequately achieve good quality chest compressions.

It is interesting to note that unlike in Perberdy's and other similar studies,^{15,16} our male participants had a lower depth of chest compression without feedback. It may be because there may be a fear among the males that having a greater muscle mass and strength,¹⁷ they may injure the victim if they push with too much force and thus practice restraint. With feedback, this trend was reversed, as the male participants would know if they are pushing too hard and could perform compressions without undue worry.

A limitation of the study would be the lack of randomisation of the order of CPR with and without feedback. There may be an element of "learning" whereby after the first attempt at CPR the performers get better because of practice and the study could have been improved with randomisation of the order of the intervention and control.

The ILCOR published a new set of CPR guidelines in 2010¹⁸ and recommended that chest compression depth should at least be 5 cm and that the rate should be more

Table 5. Mean Compression Rate and Depth with and Without Feedback

	Mean Compression Rate (cpm)							Mean Compression Depth (cm)					
	Without feedback				With feedback			Without feedback			With feedback		
	n	Mean	Std Deviation	P Value	Mean	Std Deviation	P Value	Mean	Std Deviation	P Value	Mean	Std Deviation	P Value
Gender				0.788			0.069			0.011			0.858
Female	158	104.74	13.67		102.38	9.34		4.93	0.73		4.90	0.68	
Male	51	105.34	14.08		99.38	12.37		4.61	0.91		4.92	0.71	
Age group (years)				0.522			0.589			0.645			0.869
20 to 29	85	106.51	12.64		102.47	10.49		4.77	0.74		4.92	0.68	
30 to 39	88	103.85	13.83		101.62	9.42		4.92	0.84		4.92	0.69	
40 to 49	28	102.97	17.25		100.15	12.09		4.90	0.76		4.91	0.78	
≥50	8	105.84	10.44		98.46	9.25		4.78	0.75		4.71	0.55	
BCLS				0.382			0.569			0.160			0.622
Trained	188	105.17	13.72		101.78	9.96		4.88	0.77		4.92	0.68	
Not trained	21	102.40	14.00		100.44	12.51		4.76	0.90		4.84	0.77	
AED				0.464			0.056			0.465			0.309
Trained	177	105.19	13.81		102.22	10.32		4.87	0.77		4.89	0.70	
Not trained	32	103.25	13.45		98.48	9.14		4.76	0.86		5.02	0.60	
Attended to cardiac arrest cases				0.443			0.870			0.511			0.180
Yes	29	106.71	11.70		101.94	12.44		4.76	0.85		4.75	0.77	
No	176	104.60	14.05		101.60	9.85		4.87	0.78		4.94	0.67	
Profession				0.806			0.942			0.448			0.540
RN	122	105.25	14.20		101.49	10.07		4.90	0.78		4.89	0.70	
EN	62	104.84	13.70		101.73	10.38		4.84	0.79		4.98	0.65	
Others	25	103.26	11.79		102.25	10.88		4.68	0.81		4.81	0.72	
Qualification				0.045			0.004			0.915			0.390
Diploma	70	108.55	12.06		103.72	10.05		4.88	0.79		4.87	0.70	
Advance Dip	20	104.56	9.77		105.23	9.51		4.93	0.79		5.02	0.72	
Degree	99	102.15	15.32		99.32	9.97		4.83	0.81		4.90	0.69	
NITEC	12	105.81	11.02		101.05	10.41		4.77	0.65		5.10	0.64	
Others	4	110.44	11.37		112.60	9.65		4.58	0.82		4.37	0.42	

BCLS: Basic Cardiac Life Support; AED: Automated External Defibrillation; RN: Registered Nurse; EN: Enrolled Nurse

than 100 per minute. As the study was conducted before the publication of the 2010 guidelines, the targets were those of the 2005 guidelines. Our feedback devices were prompting to the 2005 but not the 2010 guidelines. However, by calibrating the feedback devices in accordance with 2010 guideline targets, they can be used for CPR and we would expect the results to be similar, though such a conclusion must be borne by another study using the new chest compression guidelines.

We intend to follow up on this study by performing a comparison on whether these devices make a difference in rates of return of spontaneous circulation and survival during real cardiac arrest situations.

Conclusion

In conclusion, the use of real time audiovisual feedback during chest compression training with manikins improves the quality of CPR. We recommend the use of audiovisual feedback during training and during actual CPR to improve the quality of CPR. More studies are required to show that audiovisual feedback devices can improve survival in patients with cardiac arrest receiving CPR.

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Percutaneous Transluminal Angioplasty of Transplant Renal Artery Stenosis

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Abstract

Introduction: This study aimed to assess the outcome of percutaneous transluminal angioplasty (PTA) as the primary treatment for transplant renal artery stenosis (TxRAS). **Materials and Methods:** A retrospective review of PTA of TxRAS from April 1999 to December 2008 was performed. Twenty-seven patients (17 males (M):10 females (F)) with the mean age of 49.5 years underwent PTA of TxRAS in the review period. Indications for PTA were suboptimal control of hypertension (n = 12), impaired renal function (n = 6) and both suboptimal control of hypertension and impaired renal function (n = 9). All patients had doppler ultrasound scans prior to their PTA. In addition, 5 of these patients had computed tomography angiography (CTA) and another 7 had magnetic resonance angiography (MRA) evaluation. Mean follow-up period was 57.0 months (range, 7 to 108 months). **Results:** The stenotic lesions were located proximal to the anastomosis (n = 2), at the anastomosis (n = 15), and distal to the anastomosis (n = 14). Technical success rate was 96.3%. One case was complicated by extensive dissection during PTA, resulting in subsequent graft failure. The overall clinical success rate was 76.9%. Seven out of 26 patients had restenoses (26.9% of cases). These were detected at a mean of 14.3 months post angioplasty (range, 5 to 38 months). All 7 patients underwent a second PTA successfully. Three of these patients required more than 1 repeat PTA. **Conclusion:** PTA is safe and effective in the management of symptomatic TxRAS and should be the primary treatment of choice. Close surveillance for restenosis is required and when diagnosed, re-angioplasty can be performed.

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Key words: Post transplant hypertension, Kidney transplantation, Transplanted kidney failure

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Introduction

Renal transplantation has become a successful means of treatment for patients with end-stage renal failure. However, in patients with kidney transplants, graft dysfunction can occur as a result of transplant renal artery stenosis (TxRAS). This can present with raised creatinine levels or as refractory hypertension resulting in increased use of anti-hypertensive drugs.¹ The incidence of renal artery stenosis in transplant kidneys is quoted as between 1% and 23%.² The prevalence of arterial stenosis affecting renal grafts has increased in recent years due to the use of marginal donors and older recipients. TxRAS usually occurs between 3 months and 2 years after transplantation, but earlier or later presentations are not uncommon.¹ Colour doppler ultrasound is used as a screening tool for TxRAS, but angiography remains the gold standard for diagnosis.³

Over time, with lesion progression, TxRAS may lead to allograft loss. Early detection of TxRAS is therefore essential in ensuring long-term graft survival. Percutaneous transluminal angioplasty (PTA) has become established as the primary treatment of choice in TxRAS over the last 2 to 3 decades since initial reports in the late 1970s.⁴ The objective of this study is to report on our local experience by assessing the outcome of patients that have undergone PTA of TxRAS at our institution over a 9-year period.

Materials and Methods

This retrospective study was performed with the approval of our institutional review board. All patients who underwent PTA of TxRAS between April 1999 and December 2008 at our institution were identified. We collected data from 27 patients (17 males and 10 females) by reviewing their

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medical records. Their ages ranged from 29 to 63 years old with a mean of 49.5 years. All patients received the allograft kidney from a cadaveric donor except for 1 patient who had a living-related transplant. The underlying cause of renal failure was chronic glomerulonephritis in 20 patients; adult polycystic kidney disease in 3 patients; hypertensive nephrosclerosis in 1 patient; diabetic nephropathy in 1 patient; and unknown in 2 patients. With regard to vascular risk factors, dyslipidemia was present in 14/27; diabetes mellitus in 9/27; ischaemic heart disease in 3/27; and hypertension in 25/27 patients. All were cytomegalovirus (CMV) positive. Six patients had a history of acute rejection—5 of these had 1 episode of acute rejection each; the remaining patient had several episodes of acute rejection. The average time of presentation of TxRAS from transplant varied from 1 to 188 months (mean 51.1 months). A trial of conservative treatment would typically be implemented following the initial diagnosis. A decision was made for PTA if there was failure of conservative treatment. The average time from diagnosis to PTA ranged from 0.2 to 35 months (mean 5.8 months).

The indications for PTA included suboptimal control of hypertension only ($n = 12$), impaired renal function only ($n = 6$), and both suboptimal control of hypertension and impaired renal function ($n = 9$). Impaired renal function was defined as a persistent rise in serum creatinine by 20% or more. Suboptimal control of hypertension was based upon the assessment of the referring nephrologist. All patients had doppler ultrasound scans performed prior to their PTA. In addition, 5 of these patients had computed tomography angiograms (CTA) and another 7 had magnetic resonance angiography (MRA) evaluation following the initial Doppler ultrasound.

Informed consent was obtained from all patients prior to intervention. Diagnostic renal arteriography was performed via a femoral arterial approach; an ipsilateral or contralateral approach was chosen based on the type of surgical anastomosis of the transplant renal artery (end-to-side with use of the external iliac artery or end-to-end with use of the internal iliac artery) and the angle of the anastomosis. Eighteen patients had an end-to-side anastomosis with the external iliac artery (66.7%). The other 9 patients had end-to-end anastomosis with the internal iliac artery (33.3%). If there was concern for contrast material-induced nephrotoxicity, alternative contrast agents (e.g. carbon dioxide and gadolinium) were used for preliminary angiography in selected patients. Carbon dioxide was utilised in 5 procedures and gadolinium in 5 procedures to reduce the volume of iodinated contrast administered. Of these, 2 of the procedures where gadolinium was utilised were performed in the same patient. Gadolinium was utilised prior to the discovery of nephrogenic systemic fibrosis (NSF) as a possible complication in renal impaired

patients.⁵ On follow-up of a mean of 59.5 months (range, 19 to 78 months), none of the 4 patients have since developed NSF. We now no longer use gadolinium contrast medium in renal impaired patients.

The volumes of iodinated contrast material were kept to a minimum to reduce the risk of nephrotoxicity. After appropriate calibration of the images, measurement of stenosis was made by measuring the ratio between the diameter of the stenosed segment of the artery and the diameter of a normal segment of renal artery. A stenosis was considered to be haemodynamically significant when there was 50% or more narrowing of the luminal diameter on angiography or greater than 10% peak systolic pressure gradient across the lesion. When a decision was made to proceed with PTA, an appropriate guiding sheath was inserted and heparin sodium was administered intra-arterially (2000 to 3000 International Units). The stenosis/stenoses were traversed with a guidewire, followed by the use of 4 French catheters to obtain pressure measurements across the lesion. A range of guidewires was utilised depending on the anatomy of the lesion, and included 0.035", 0.018" and 0.014" wires. Nitroglycerin (100 to 200 ug intra-arterially into the transplant renal artery) was administered to prevent vasospasm on an operator preference basis. The size of the balloon was chosen to oversize the measured diameter of the normal segment of the renal artery by no more than 1 mm. The balloon was inflated across the lesion at nominal pressure for approximately 1 minute. A post PTA angiogram was performed to check for residual stenosis (Fig. 1). Technical success was defined as residual stenosis of less than 30% after PTA and with no flow-limiting intimal flap. Following the procedure, the patients were started on oral aspirin therapy (100 mg daily).

The blood pressure (BP), number of anti-hypertensive drugs and serum creatinine were closely monitored after PTA. Clinical adverse events post-procedure were recorded to assess the complication rate. The patients had a baseline Doppler ultrasound 2 weeks post PTA followed by 6-monthly, then 12-monthly surveillance scans thereafter.

For patients treated for suboptimal control of hypertension, clinical success was defined as normalisation of BP or a reduction in diastolic BP by more than 15 mm Hg and/or reduction in the number or dosage of anti-hypertensive drugs. For patients treated for impaired renal function, clinical success was defined as a serum creatinine reduction of 15% or a less than 15% change from baseline serum creatinine.⁶

Results

The stenotic lesions treated were located proximal to the anastomosis in 2 patients; at the anastomosis in 15 patients; and distal to the anastomosis in 14 patients. Four patients had

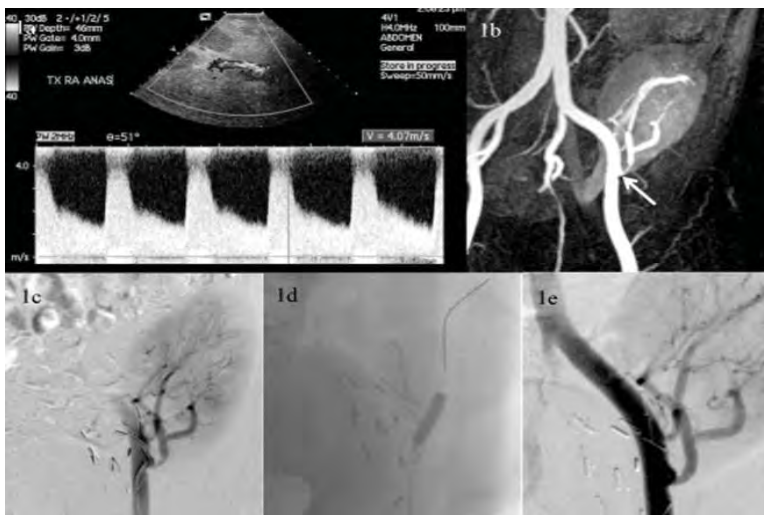


Fig. 1. Case of a 50-year-old male with a 1-year-old transplant allograft. (A) Ultrasound doppler showed peak systolic velocity (PSV) of more than 4 m/second of the transplant renal artery. (B) Contrast enhanced MRA confirmed TxRAS at the anastomotic site (arrow). (C) Angiogram via the ipsilateral femoral approach confirmed a 75% TxRAS. (D) PTA performed with 5 mm x 20 mm angioplasty balloon. (E) Post PTA angiogram demonstrated a good result with 20% residual stenosis.

more than one segment of stenosis. We used an ipsilateral approach in 9 patients and a contralateral approach in the remaining 18 patients. The sizes of the angioplasty balloons utilised ranged from 3 mm to 8 mm in diameter.

Immediate technical success was achieved in 96.3% of the cases (26 out of 27 patients). The only technical failure was in a patient with a 15-year-old graft, where the procedure was complicated by extensive dissection and surgical exploration had to be performed immediately on the patient (Fig. 2). At surgery, the extensive dissection was confirmed, but it was also noted that the recipient left internal iliac artery and the allograft arteries were diffusely diseased due to atherosclerosis. A surgical bypass was created across the dissected segment but in spite of that, the allograft could not be salvaged and the patient had to resume haemodialysis.

One patient had a moderate dissection post PTA that was treated by stenting (Fig. 3). Another patient had a moderate groin haematoma that resolved with conservative treatment.

In the 26 patients who had successful PTA, the mean follow-up was 57.0 months (range, 7 to 108 months). Post PTA, there was a significant reduction in BP in 12 patients. The BP remained stable in 13 patients, while

there was worsening of BP in the remaining patient. The number of anti-hypertensive medications decreased in 10 patients and remained unchanged in 14 patients (5 of these patients had the dosage of the existing number of drugs reduced). In the remaining 2 patients, the number of anti-hypertensive medications increased. In 1 of the 2 patients, the BP remained stable following the increase in number of medications by 1 additional drug and no repeat procedure was undertaken. In the second patient, the BP continued to worsen following PTA due to re-stenosis, thus increasing the requirement for anti-hypertensive drugs from 3 to 4. However, the patient was not keen for a repeat PTA and was thus managed conservatively.

At 6 months after PTA, the serum creatinine improved by more than 15% in 6 patients (23.1%), remained stable in 19 patients (73.1%) and worsened by more than 15% in 1 patient (3.8%). Twenty-two of 26 patients had follow-up of 1 year or more. At 1 year following PTA, the serum creatinine improved by more than 15% in 8 patients (36.4%) and remained unchanged in 9 patients (40.9%); the serum creatinine worsened by more than 15% in 5 patients (22.7%). The overall clinical success rate was therefore 76.9% (20 out of 26 patients). Of the poor clinical success patients, 2 initially presented with hypertension; 2 with elevated

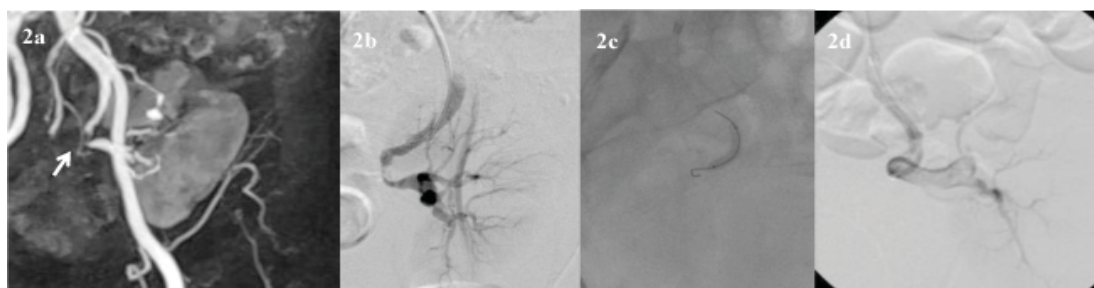


Fig. 2. Case of a 57-year-old woman with a 15-year-old allograft. (A) MRA showed a severe stenosis at the transplant artery anastomosis (arrow). (B) Pre PTA angiogram confirmed a severe 95% TxRAS with intrarenal arterial disease. (C) PTA performed with a 4 mm x 20 mm angioplasty balloon. (D) Post PTA angiogram showed severe flow limiting dissection that could not be salvaged.

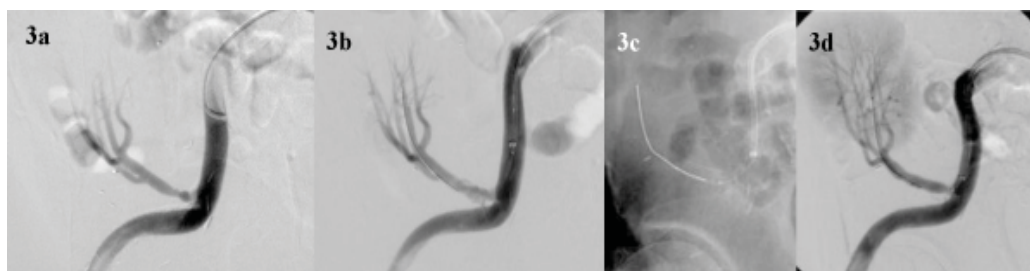


Fig. 3. Case of a 55-year-old man with a 2-year-old allograft. (A) Angiogram showed a 70% focal stenosis of the proximal transplant renal artery. (B) Post PTA angiogram demonstrated a moderate dissection that was resistant to redilatation. (C) A 6 mm x 18 mm balloon expandable stent was deployed across the lesion. (D) Post stenting angiogram shows successful treatment of the dissection with no residual stenosis.

creatinine and 2 with both hypertension and elevated creatinine. However, 4 out of the 6 poor clinical success cases had a history of acute rejection.

Seven out of 26 patients (26.9%) had restenoses of the TxRAS on follow-up. These were detected at a mean of 14.3 months post PTA (range, 5 to 38 months). Two patients had an end-to-side anastomosis; the rest had an end-to-end anastomosis. All cases of restenosis occurred in cadaveric allografts. None of the restenosis patients had episodes of acute rejection. None of the patients with poor clinical success presented with restenosis on follow-up.

All 7 were successfully treated with a repeat PTA. Two patients had stents inserted during the repeat PTA due to early restenosis. Three of the patients who had restenosis required more than 1 repeat procedure. Two patients required 2 repeat PTAs while the remaining patient had 3 procedures. A total of 38 procedures were performed in 27 patients. All the patients who underwent repeat PTA had stable renal function except 1. She eventually lost the function of her allograft 42 months after the second repeat PTA due to chronic rejection. One patient died from pneumonia 8 months after the second repeat PTA.

Discussion

TxRAS is not uncommon after renal transplantation, and it should be considered in patients who have worsening hypertension and/or renal dysfunction. The most common causes of stenosis are 'technical' where the stenosis occurs due to surgical technique, usually located at the anastomosis and especially at the end-to-end anastomosis. This may be due to trauma during kidney harvesting and transplantation, or less commonly, as a result of the anastomosis being too tight. Kinking or angulation of the artery is another possibility.⁷

CMV infection can also contribute to the development of TxRAS by causing proliferation of vascular cells, including endothelial cells, neointimal cells and smooth muscle. This effect may in part be due to inhibition of p53 by viral gene products.⁸ Recipients who were CMV negative

and then became CMV positive after transplantation had a significantly higher prevalence of TxRAS versus those who remained seronegative.⁹

Immunological injury has also been proposed as a possible cause, especially in diffuse and multiple stenoses. Intimal proliferation was associated with chronic rejection prior to the introduction of cyclosporine, but no consistent correlation has been found between acute rejection and TxRAS.¹⁰ In our study, 6 patients were complicated by acute rejection (22.2%) but only 2 of them had more than 1 segment of stenosis. In addition, this may be confounded by positive CMV serology in all 6 patients.

Stenosis can also occur due to atherosclerosis of the donor renal arteries or recipient iliac arteries, or both.¹⁰ A haemodynamic mechanism has been suggested in end-to-side anastomosis, with angulation between donor renal artery and the recipient iliac artery leading to turbulent blood flow.^{7,9} In our study, 18 out of 27 patients had an end-to-side anastomosis. However several studies have shown no difference in the prevalence of TxRAS between the end-to-side and end-to-end techniques.⁹

A higher incidence of TxRAS is reported in cadaveric transplants (range, 13.2% to 17.7%) compared with live donors (range, 1.3% to 5.8%).¹⁰ Greater cold ischaemia time, which is inevitable in cadaveric transplants, is compounded by the use of pulsatile perfusion systems that may contribute to endothelial damage in the renal artery.⁹ The majority of our cases were in patients with cadaveric allografts (26 out of 27). However this may also be a result of cadaveric transplants being more prevalent than living-related transplants in the local setting. Cyclosporine has also been suggested as a cause for TxRAS by inducing endothelial injury leading to the development of a stenosis. However no studies have been conclusive.¹⁰

Early TxRAS that occurs within a few months of surgery is likely secondary to technical causes or trauma whereas TxRAS developing more than 6 months following surgery cannot be as readily explained and may be associated with the progression of underlying atherosclerosis.¹⁰

There are 3 main types of TxRAS: (i) stenosis at the

anastomosis; (ii) localised stenosis, proximal or distal to the anastomosis; and (iii) diffuse or multiple stenoses.⁷ Preanastomotic arterial stenoses are usually due to atherosclerosis or clamp injuries while stenoses at the anastomosis are usually due to technical problems related to surgery. Stenoses distal to the anastomosis are usually due to immune reactions or haemodynamic turbulence from the anastomosis leading to intimal hyperplasia. Intrarenal distal stenoses, on the other hand, are usually due to chronic rejection. Post anastomotic stenoses tend to be more severe and more frequently associated with end-to-side anastomoses compared to end-to-end anastomoses, which tend to be at the anastomoses.¹⁰

PTA has been for years considered the initial treatment of choice for TxRAS as it does not preclude subsequent surgical correction. The technical success of PTA for TxRAS has been reported in 70% to 90% of the cases with a low complication rate. Our results of technical and clinical success are comparable to those quoted in the literature.^{1,9,11-15} We noted that 4 out of the 6 cases of poor clinical success had a history of acute rejection. This may be a possible cause for our discrepancy between technical success and clinical success rates. Restenosis rate after PTA alone has been quoted as between 16% and 62%.¹¹ The restenosis rate in our patients (26.9%) falls within this range. PTA is considered to be more favourable compared to surgical intervention, which carries increased risk of graft loss as well as ureteral injury.^{10,15} Transplant patients are also poor surgical candidates in general because of their chronic immunosuppressed state.⁴

There are a few limitations in our study. Firstly, as the study is retrospective, the follow-up protocol post PTA may not be strictly standardised. The number of patients in our study is also relatively small, but this can be attributed to the low incidence of this condition among our renal patients. Another limitation is that for the purpose of this study, we utilised serum creatinine as the marker of renal function. A more accurate assessment of renal function would have been the glomerular filtration rate (GFR). GFR was however not a standard utilised in our clinical practice during the earlier part of the study period. It was not possible to obtain the patients' weights at the time points of the serum creatinine results due to the retrospective nature of our study. However, most studies in the literature assessing the success of PTA in TxRAS have utilised serum creatinine as the marker for renal function.^{1,9,12,15}

Metallic stents can be inserted for the treatment of recurrent or ostial stenoses. Stenting is associated with high initial technical success and a good patency rate with minimal complications.¹⁰ Many recent reports highlight the role of PTA with stenting in limitation of recurrence, leading some authors to suggest stent implantation at the first angioplastic procedure.¹¹ However limited studies

have been reported to date and there is a lack of data on the long-term outcome and complications of stenting in TxRAS. In our study, only 3 patients required stenting, 1 for dissection, and 2 for restenosis. Based on our experience, we do not feel that primary stenting is justified, and further studies will need to be performed comparing stenting to repeated angioplasties.

Conclusion

Our experience shows that PTA is safe and effective in the management of symptomatic TxRAS and should be the primary treatment of choice. Close surveillance for restenosis is required and when diagnosed re-angioplasty can be performed effectively.

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Changing Landscape of Nursing Homes in Singapore: Challenges in the 21st Century

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Abstract

The ageing population is posing new challenges to Singapore's healthcare system. The rise of dual income and the decline of extended families, as well as an increase in age-related degenerative disorders due to increased longevity render it difficult for the family to remain the primary social safety net to care for our elderly in their own homes. Consequently, nursing homes may become increasingly relevant for resource and expertise-challenged families to cope with the burden of caring for a frail and dependent elderly. However, as the recent Nightingale Nursing Home elderly mistreatment incident attests, the standards of some have been found wanting. This paper will trace the history of nursing homes in Singapore and the evolution of government policies towards them, discuss the challenges and trade-offs of nursing home regulation, and provide suggestions for better care and governance.

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Key words: Elderly, Humanistic, Long-term care, Person-centred

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Abstract

The ageing population is posing new challenges to Singapore's healthcare system. The rise of dual income and the decline of extended families, as well as an increase in age-related degenerative disorders due to increased longevity render it difficult for the family to remain the primary social safety net to care for our elderly in their own homes. Consequently, nursing homes may become increasingly relevant for resource and expertise-challenged families to cope with the burden of caring for a frail and dependent elderly. However, as the recent Nightingale Nursing Home elderly mistreatment incident attests, the standards of some have been found wanting. This paper will trace the history of nursing homes in Singapore and the evolution of government policies towards them, discuss the challenges and trade-offs of nursing home regulation, and provide suggestions for better care and governance.

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Introduction: Nursing Home's Evolution

Nursing homes trace their evolution to American almshouses in the 1930s where retired nurses welcomed the elderly and ill into their homes.¹ In Singapore, community-based charitable organisations pioneered the earliest sheltered accommodations for homeless and destitute elderly immigrants. For instance, the local chapter of the Little Sisters of the Poor founded St Theresa's Home in 1935 to provide accommodation, food, clothing and other services to the elderly.² Well known social worker, Teresa Hsu, also founded one of the earliest nursing homes, the Home for the Aged Sick at Jalan Payoh Lai, in 1965.³

Concerted social welfare programmes began after the Japanese Occupation to cater to the large swathes of displaced population. As the population resettled, welfare services grew to provide palliative, remedial and protective functions. While initially it was juvenile delinquents and commercial sex workers who were placed in welfare homes, they eventually evolved to encompass the sick and elderly. In 1959, the City Council and Rural Board passed the Nursing Homes and Maternity Homes Registration Ordinance to govern such homes.⁴ Post-independence,

1966 Parliamentary Records document Minister of Health, Yong Nyuk Lin, citing the Trafalgar Home for Lepers as a means to "relieve congestion" for the adjacent Woodbridge Hospital. This marked welfare homes' incorporation into national healthcare considerations. Thereafter, psychiatric rehabilitation homes provided residential care for patients who no longer required active treatment but needed training to readjust to society. Construction of the earliest psychiatric halfway home in Sembawang began in the 1970s and channelled recovering patients from Woodbridge Hospital.⁵

During this period, the practice was applied to eldercare with the formation of homes for the aged, although they were limited in number.⁶ Such nursing homes included the Singapore Christian Home, set up in the 1960s, and the Methodist Home for the Aged Sick in 1983.⁷ The first government-directed nursing home initiative was the conversion of a disused school in Woodlands into Woodlands Home for the Aged. Conditions of these early homes were spartan; they were built dormitory-style and only had toilets at the end of each block.

In 1983, Woodbridge Hospital established the Chronic Sick Unit for the chronically ill to free acute care beds

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and centralise chronic care.⁸ As homes for the aged lacked expertise and resources to care for elderly with chronic illnesses, many were sent to the Chronic Sick Unit for treatment. Ironically, when the patients recovered, families were reluctant to discharge them given the low ward charges at the unit.⁸ It thus became a long-term care facility for some patients.

Despite all the activity, government policy towards homes for the aged was minimal. In 1976, Dr Tan Eng Liang, the Minister of National Development, broached the renting of Housing and Development Board (HDB) flats to homes for the aged to house the elderly as “old family traditions (were) breaking down”.⁹ The idea, however, received little traction. Instead, the government focused on a code of conduct for nursing homes. The Ministry of Health’s 1981 Guideline recommended nursing homes set out standards for care to be reported to the Director annually and mandating they should have written policies, guidelines for hygiene. Besides stringent regulation on advertising, most guidelines were discretionary and aimed towards proper book-keeping and reporting.

The lack of alternative community-based care options such as day care, rehabilitation and therapy services left nursing homes as the most viable option for care of the chronically-sick elderly. Families who wanted to care for their elderly at home received limited practical help, medical or financial support, and the much-lauded Central Provident Fund (CPF) was created only after 1983. As noted by the 1991 Health Review Committee on National Health Policy, health for the elderly was one of the 5 inadequately supported aspects of Singapore healthcare which necessitated the “channelling of more resources”.¹⁰

In the 1984 Report of the Committee on the Problems of the Aged, homes for the aged were broadly classified into 2 categories: for the destitute elderly; and the sickly elderly.¹¹ The government would be responsible for the former, under the then Ministry of Community Youth and Sports (MCYS), while voluntary welfare organisations were encouraged to set up and manage homes for the latter with assistance from the Ministry of Health (MOH) to ensure they were “adequately and efficiently managed”. In 1989, Parliament enacted the Homes for the Aged Act to govern nursing homes. It grants power to the Director to issue, transfer or to terminate nursing homes’ licenses and demand that nursing homes furnish him with relevant information. Refusal would be subject to a \$2000 fine.¹²

Society’s ethos emphasising filial piety persuaded government policy to prioritise familial support over nursing homes for care of the elderly. When the 1999 Inter-Ministerial Committee on Health Care for the Elderly noted the undersupply of facilities, the government continued to hold back nursing home numbers as it believed families

would be “affected negatively” if nursing homes were readily available as they discouraged families from caring for the elderly themselves.¹³

Nursing homes gradually faded from legislative and public consciousness, albeit with occasional mention. For example, in a parliamentary debate about means testing, the issue of “disparity” in standards between nursing homes and community hospitals was raised.¹⁴ However, without the necessary impetus, there was no concerted effort to re-examine policy towards nursing homes. Eventually, an ageing population and hospital overcrowding revived nursing homes’ importance. Declining birth rates and increased life expectancy increased the burden on a dwindling supply of caregivers, while a shortage of facilities for the chronically ill threatened a “bed crisis”. In response, the government, increased grants and subsidies for voluntary welfare organisations to construct and maintain nursing homes; and released 17 tender sites for private companies to set up nursing homes.¹³

In the 1990s, to encourage the growth of nursing homes, the government provided generous subsidies to voluntary welfare organisations (VWOs) to run nursing homes of up to 90% of capital costs for construction and continuing subsidy of 50% of operating costs. The government also emulated Australia in introducing categorisation for elderly patients into 4 classes based on time-motion studies of the resources needed to perform care procedures, and gave strong financial and subsidy incentives to encourage nursing homes to take on patients with higher medical needs and increased dependency (Category III and Category IV), thereby introducing the medical facet to nursing home care.

To further expand the residential eldercare sector, the government demolished the Woodlands Home for the Aged and constructed 3 homes in its place under the purview of MCYS: Christalite Methodist Home for the Aged, Bukit Batok Home for the Aged, and Jamiyah Home for the Aged. Compared to their predecessor, these new homes had upgraded amenities and improved care capabilities with communal areas for socialisation, gathering points for volunteers and social programmes for residents. Being primarily homes for the destitute elderly, this heralded a paradigm shift towards a more holistic and well-rounded living environment in long-term care for the elderly. Gradually, more support came from the community whereby companies would sponsor red packets for residents and doctors volunteered their time at the facilities.

However, not all efforts were smooth sailing. Attempts to introduce audits in the 1990s, with a view to improve clinical care, were met with some resistance from nursing home operators who felt it threatened their established modes of operation. As a result, such efforts never really took root. Workforce shortages also meant nursing homes

were increasingly reliant on foreign workers, which in 2011, constituted 25% of the total healthcare workforce,¹⁵ with a larger proportion of foreigners in long-term care settings. Meanwhile, nursing home jobs remained unattractive to locals due to long working hours and modest remuneration. The foreign worker levy for nursing homes was waived in an attempt to address the problem, allowing homes to bring in foreign labour at cheaper costs.¹⁶

However, recent events brought to light the lack of quality care at some nursing homes. The Nightingale Nursing Home incident, where employees were filmed mistreating an elderly patient,¹⁷ highlighted nursing homes' dubious employment practices and the difficulties in monitoring and regulation. In 2012, there were, in total, 9 reported complaints of abuse by nursing home staff mainly pertaining to rough handling, particularly, during patient transfers.¹⁸ Intuitively, the possibility of under-reporting is high.

To compound matters, the construction of nursing homes near property also aroused public displeasure. One, at Bishan Street 13, stirred nationwide conversations when residents in the vicinity petitioned the government to have it situated elsewhere, claiming decreased ventilation would raise utility charges and they would have elderly "groaning" into their homes.¹⁹ This has been termed the not-in-my-backyard (NIMBY) syndrome, and highlights the lack of societal support and acceptance for nursing homes.

Current Policy Towards Nursing Homes

Nursing homes are part of the wider eldercare initiatives that include ElderShield, services that encompass befriending, home help and respite care, and public education campaigns like the active ageing initiative. "Ageing in place" are buzz words today as more initiatives are rolled out to facilitate senior citizens in maintaining wellness and independence, and supporting those with disabilities with services in the community so as to enable them to continue living in the comfort of their own homes instead of the nursing home. Community-based services also have the advantage of reduced cost compared to institutional care. Information on the different types of eldercare services and their respective locations around the island can be conveniently found on the ElderCare Locator of the Silver Pages of the Agency for Integrated Care (AIC).²⁰

Nonetheless, despite efforts to help seniors age in place, it is projected that Singapore will need up to 15,600 nursing home beds by 2020 from the present 9300 thereabouts²¹ to cater to the frail elderly with high care needs. The government employs a "many helping hands" approach towards nursing homes, engaging a diversity of external partners, ranging from VWOs to private operators to construct and operate nursing homes. The diversity allows different nursing homes to cater to different niche segments

of the elderly population.

To aid in allocation, elderly patients are classified into 4 categories by the Resident Assessment Form: Category I patients are physically and mentally independent; Category II patients are semi-ambulant; Category III patients are wheelchair or bedbound; and Category IV patients are highly dependent. Category I and II patients are primarily admitted to sheltered homes, while the limited nursing home places are mainly reserved for Category III and IV patients. Category II patients may be admitted to nursing homes, but intake is highly restricted and capped.²²

The Private Hospitals and Medical Clinics (PHMC) Act and Regulations, and Specific Guidelines for Nursing Homes, enacted in 1981 and 1990²³ allow nursing homes to determine the standard and system of care, with regular reporting to the Ministry. It, however, maintains strict restrictions on advertising and promotions, restricting "testimonials by...patients", "any mention...of personal skills of doctors", "comparisons...between one nursing home and another" and generally "any sales promotions".²³ Such restrictions are meant to limit nursing homes' appeal to Singaporeans. Instead, the government encourages co-residence between children and ageing parents as a financial arrangement and moral obligation.²⁴

To operate, nursing homes must receive 2-yearly licences from the Ministry, subject to yearly formal inspections. In the light of the Nightingale Home incident, Minister of State for Health, Dr Amy Khor, proposed a "Visitors Programme" where volunteers would visit nursing homes and interview patients and family members, before submitting a report back to the Ministry.¹⁸

To help reduce the government's financial burden of running nursing homes and ensure "shared responsibility", in line with the 1981 National Healthcare Plan, patients' families have to pay part of the costs of their stay and treatment. Patients from households with under \$2200 per capital monthly income would have a subsidy range from 10% to 75%. These patients may be further covered under ElderShield, helping defray costs of long-term costs.²⁴ For financially able households, they would have to pay the full fee estimated at \$2000 monthly. However, there has been criticism that the subsidies are inadequate and the monthly income cap is inflexible and insufficient, given inflation.

Recently, the government has attempted to remake nursing homes to be more liveable through incorporation of greenery and communal spaces into the design, and greater emphasis on attending to the social needs of residents. New standards for nursing homes are expected by 2015 and homes are also encouraged to "expand their services" to offer day care and rehabilitation services to the wider elderly community.²⁵ In the future, the government plans to aggressively expand nursing home numbers and bed

space, building 10 new nursing homes and complementary day care, dementia day care, day rehabilitation services by 2016.²⁶ Such facilities will be well connected to the areas in the vicinity to involve the community in eldercare and create elderly-friendly neighbourhoods.

Challenges of Legislating Nursing Homes in Singapore

In regulating nursing homes, the government faces several quandaries. Firstly, it must balance the risks of under-regulation and over-regulation. While the risks of the former are clearly manifest in the Nightingale Home incident, the latter risks raising costs for both operators and consumers, and even driving some below par nursing homes out of business, compounding the already severe shortage of bed space for the chronically ill.²⁷

Secondly, it must weigh the risks of an increasing reliance on nursing homes undermining traditional values of filial piety. Fan et al argues that a “promotion of filial piety values” could be a “solution” to an ageing population²⁸ which includes caring for one’s elderly parents. Nursing homes could potentially encourage children to abrogate this responsibility. However, they are also essential for the chronically or terminally ill, as families often lack the resources and expertise to care for them, and ill-equipped caregiving risks decreasing patient’s quality of life and adds stress to caregivers. It is becoming increasingly clear that with smaller and dual income families, relying only on families as the social safety net may no longer be tenable. There is a need to enhance safety nets within the community and nursing homes play a pivotal role in this respect.

Lastly, the government must also consider the implications of further privatisation of the nursing home industry. The current system is a tenuous balancing act between voluntary and commercial operators, with 4979 patients in the former, and 3039 in the latter,²⁹ although tight advertising regulations restricts the ability of commercial nursing homes to differentiate services and build consumer awareness. However, further privatisation provides distinct advantages in allowing market forces to influence operators to enhance industry efficiency in lieu of supply and demand. It would also accord greater flexibility and allow the development of niche areas to cater to dynamic changes in consumer demand. As Wunderlich and Kohler observed, current long-term care recipients often lack a “choice” of providers or services, limiting the efficaciousness of market forces in upholding standards.³⁰

However, as the availability and quality of nursing homes is a public good, with externalities on the wider healthcare system, unfettered market forces alone should not govern its supply. The lack of effective regulation to deter errant behaviour and ensure minimal standards further increases the risks of moral hazards and poor quality care. It is also

morally dubious to create a system where only the well-off have access to nursing homes. Furthermore, expansion of the nursing home sector by the private sector may risk diluting standards and increase the complexity of auditing and regulation.

Recommendations

To tackle these problems, firstly, a calibrated approach to increasing regulatory oversight and standards of care could be introduced. A basic evidence-based education outreach programme to impart and reinforce vital caregiving skills could be conducted for nursing home staff where “oral and visual information” are disseminated via PowerPoint presentations and brochures to medical professionals, which Bernal-Delgado et al suggests is “incrementally more effective” than conventional outreach.³¹ Lectures via video conferencing as part of an overall telemedicine initiative can serve this purpose well. In conditions that require specialised care such as dementia, there often lies the issue of providing specialised dementia homes versus up-skilling all nursing homes to care for residents with dementia. Both approaches can be adopted, whereby all nursing homes should have staff with skills to manage dementia but at the same time, there should also be homes specialising in dementia care to care those with higher needs such as difficult to manage behaviours.

To increase accountability and incentivise good care, end-of-life elements could be introduced into nursing home’s clinical audit as recommended by the National Strategies for Palliative Care Workgroup,³² and surveying families upon patient demise on care quality, as modelled after the Toolkit of Instruments to Measure End-of-life care (TIME) from Brown University.³³ Such measures strengthen the feedback mechanism and increase nursing home accountability to patients’ families and the wider community. The current practice of displaying results of key performance indicators of various hospitals³⁴ in the public domain could be extended to nursing homes to spur competition amongst homes to upgrade standards and give families of prospective patients a more informed choice.

Secondly, improved coordination and communication between nursing homes and hospitals, and instilling a culture of continuous quality improvement could raise standards of medical care. Currently, nursing homes lack input from hospital specialists on matters of clinical care. Local studies have highlighted issues of concern such as poly-pharmacy and inappropriate medication prescriptions in 58.6% to 70% of nursing homes surveyed.^{35,36} Diminished quality of life as suggested by a significant prevalence of malnutrition, urinary incontinence, falls, functional decline and impaired vision have also been described.³⁷ Improved medical support could ameliorate the situation and this

can be realised through periodic visits by physicians and geriatric specialists or telemedicine.³⁸ Some noteworthy recent initiatives to improve long-term care quality include recommendations from the Nursing Home Expert Panel at MOH³⁹ and quality initiatives by AIC.⁴⁰

Thirdly, there could be reconsideration on the current stringent classification of elderly patients which determine the care they can receive. The current classification of patients according to the Resident Assessment Form with the attendant categorisation of homes by level of nursing capability opens up a “service gap” for some Category II patients transiting into Category III.²² As Category II patients suffer cognitive and physical decline, they need to be uprooted from assisted living facilities run by MCYS and transferred to nursing homes operating under MOH’s purview, a process that can be disruptive and distressing to the patient. Instead, eldercare facilities should ideally allow the elderly to “age-in-place”.²² Increasing the capabilities of all homes and implementing a more flexible classification system would provide more patient-centric treatment that upholds the dignity and autonomy of our elderly. It would also facilitate market creativity and potentially spawn integrated centres where patients can traverse the ageing continuum with greater comfort and security.

Additionally, in the long run, reliance on foreign nursing home staff can be gradually reduced. This can be implemented through MOH’s efforts in increasing local intake at healthcare training programmes, encouraging mid-career switches and drawing back healthcare professionals working overseas.¹⁵ There is a need to afford greater recognition to nursing home medicine as a unique discipline, enrich the academic curriculum, delineate attractive career paths, and enhance work benefits and remunerations to draw local employees. This is critical as foreign staff could experience cultural and linguistic barriers communicating with local patients, and a small minority may have inappropriate qualifications or are ill-equipped to perform their role. Hence, a core pool of local staff in nursing homes is essential to adequately meet the emotional, social and cultural needs of the elderly.

In tandem with financial incentives to support home-based care of the elderly, for instance, the Enhancement for Active Seniors Scheme which grants subsidies up to 90% for Singaporeans to make elderly-friendly modifications to their homes like grab bars and non-slip tiles,⁴¹ foreign domestic helpers can help to provide home-based care to frail elderly and serve as an alternative to foreign nursing staff. There are more than 200,000 foreign domestic workers in Singapore⁴² and recent initiatives such as a \$120 monthly grant for families to hire foreign domestic helpers to care for elderly with dementia⁴¹ are incentives to support care for the elderly at home. To increase the proficiency of

domestic helpers, the recently set up Foreign Domestic Workers Association for Skills Training⁴³ is a laudable effort.

Lastly, nursing homes could move towards humanistic and holistic care to meet increasing expectations for more privacy and higher quality of resident-centric care from better educated and more affluent generations. This is in line with the need for nursing homes to evolve alongside changing expectations of the elderly and families and would entail a shift away from current institutional-based care modelled after hospitals where the highly structured environment and centralised decision-making process may undermine patient autonomy and lead to depersonalisation, isolation and loneliness of the residents.⁴⁴

The care could be modelled after the Green House Project in the United States, which seeks to create a homely and communal residence for residents⁴⁵ with an emphasis on quality of life beyond safety and risk management. Homes could be redesigned to be more aesthetically appealing and with more recreational spaces for residents. Locally, such ideas are beginning to take root. For instance, the Hope Resident Living Area at Peace Haven Nursing Home seeks to maximise independence and autonomy for persons with early dementia.⁴⁶ It is a stellar example of what nursing home care in the future can be like. Such care would improve resident welfare by according them with more dignity, agency and respect, and merge the medical and social facets of long-term care. It would also allow nursing homes to evolve beyond its current custodial roles, towards more holistic and person centred care.

Conclusion

With nursing homes playing a central role in the future make-up of our healthcare landscape, the policies that affect and govern it will have widespread repercussions on society. While legislation was initially restrictive on nursing homes due to filial piety ethos and modest to evolve with families’ changing dynamics, population pressures have forced a policy re-think. In moving forward, Singapore must appreciate the complexity in nursing home history and the evolution of its policies, and be cognisant of the dilemma the country faces in amending policy. A clear understanding of these trade-offs would not just inform policymakers, but assist families, healthcare professionals and caregivers in making optimal choices for their ageing elderly. Hopefully, in the future, stronger regulation, improved medical care through firmer tie-ups with hospitals and physicians, and an emphasis on humanistic person centred care will make nursing homes a more attractive place to spend one’s twilight years.

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Projecting the Number of Older Singaporeans with Activity of Daily Living Limitations Requiring Human Assistance Through 2030

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Abstract

Introduction: In the context of rapid population ageing and the increase in number of activity of daily living (ADL) limitations with age, the number of older persons requiring human assistance in Singapore is likely to grow. To promote informed planning for the needs of these elderly, we project the number of resident Singaporeans 60 years of age and older with 1 or more ADL limitations requiring human assistance through 2030. **Materials and Methods:** The proportion of community-dwelling older adults with ADL limitations requiring human assistance, stratified by gender and age group, was calculated utilising a recent nationally-representative survey of older Singaporeans. The proportion of older adults in nursing homes with ADL limitations was estimated based on available literature. Together, these prevalence estimates were applied to a simulation of the future population of older adults in Singapore to derive an estimate of the number of individuals with ADL limitations requiring human assistance through 2030. **Results:** By 2030, the number of resident Singaporeans aged 60 years or older with 1 or more ADL limitations requiring human assistance is projected to be 82,968 persons (7% of the total population aged 60 years or older). Of this number, 38,809 (47%) are estimated to have 1 or 2 ADL limitations, and 44,159 (53%) are estimated to have 3 or more. **Conclusion:** The number of elderly Singaporeans with activity limitations is expected grow rapidly from 31,738 in 2010 to 82,968 in 2030. Estimates of the number of older individuals with ADL limitations requiring human assistance are of value for policymakers as well as acute and long-term care capacity planners as they seek to meet demand for health and social services in Singapore.

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Key words: Ageing, Activities of daily living, Forecasting, Long-term care, Singapore

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Introduction

Similar to other developed countries in Asia, including Japan, South Korea and Taiwan, the population of Singapore is ageing rapidly.¹ In 2011, 9.3% of the population was 65 years of age or older.² Due in part to decades of sub-replacement level fertility rates and increases in longevity, by 2030 this proportion is expected to increase to 19%.³ Given the tendency of individuals to accumulate health problems and activity of daily living (ADL) limitations as they age,⁴⁻⁶ an important consequence of this demographic shift will likely be a significant increase in demand for acute and long-term care services.⁷

A number of studies provide information on the prevalence of ADL limitations among older Singaporeans, although they vary in the instruments used to measure disability, sample size and representativeness.^{6,8,9} A recent study using data

from the Social Isolation, Health and Lifestyles Survey (SIHLS) 2009, a nationally-representative survey of 5000 community-dwelling elderly Singaporeans aged 60 years and older conducted on behalf of the Ministry of Social and Family Development (erstwhile Ministry of Community Development, Youth and Sports), reported the prevalence of having at least 1 ADL limitation to be 9.7% (12.7% for women and 6.1% for men).⁶ Of those with ADL limitations, approximately 36% had 1 or 2 ADL limitations, 24% had 3 or 4, and 40% had 5 or more. While these studies provide reasonable estimates of the current prevalence of ADL limitations among the elderly in Singapore, published studies projecting the future prevalence of such limitations are unavailable.

To assist researchers, policymakers and care planners in responding to the demands likely to be placed on health

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and social services as a result of population ageing, this paper projects, through 2030, the number of resident Singaporeans aged 60 years or older with 1 or more ADL limitations requiring human assistance. The estimates are based primarily on the age-specific prevalence from the SIHLS 2009.

Materials and Methods

Data Source and ADL Limitations for Community-dwelling Older Adults

Data pertaining to the ADL status of the SIHLS participants were utilised. Details on the design and sampling of the SIHLS are available elsewhere.⁶ In brief: single-stage stratified random sampling was employed to select the survey sample. After informed consent, a total of 5000 community-dwelling older Singaporeans aged at least 60 years or their proxy informants were interviewed face-to-face at their residence to gather information on various aspects of the older persons' physical, mental and social health.

The presence of difficulty in performing the activity (yes/no), and if yes, the type of assistance required (human/device/no assistance), was assessed for 6 ADLs (bathing or showering, dressing, eating, standing or sitting, walking around the house, and toileting) from the SIHLS participants. For each activity, those who reported presence of difficulty and required human assistance were classified as 'limitation requiring human assistance'. The weighted proportion of older adults with 1 or 2 and 3 or more ADL limitations requiring human assistance was calculated for population strata defined by gender and age (in 5-year cohorts from age 60 to 94 years and age 95 years and older). The cut-off between 2 and 3 ADL limitations was chosen because current rules for ElderShield—a government-sponsored insurance scheme that provides basic financial protection to those with long-term care needs—define the 'severely disabled' as individuals who are unable to perform at least 3 of 6 ADLs.¹⁰

Population and ADL Limitations for Institutionalised (in Nursing Home) Older Adults

The proportion of nursing home residents in 5-year age cohorts from age 60 to 95 years, and 95 years and older was estimated using information from a study by Yap et al.⁷ Since Yap et al used different age categories than those needed for the current study, the proportion of individuals in each age category reported by Yap et al was summarised as a linear regression (proportion of individuals in the age category in nursing home = (midpoint age of the age category) (1.0745) – 56.124; $R^2 = 0.87$). This regression model was used to calculate the proportion in 5-year age

cohorts from age 60 to 95 years, and 95 years and older. The estimated proportion in each age cohort was distributed by gender to match the overall gender distribution of nursing home residents (31% male and 69% female) reported by Yap et al. The resulting proportions were multiplied by the estimated total number of nursing home residents aged 60 years or more in 2010 ($n = 9082$) to arrive at the number of nursing home residents in each stratum defined by gender and age cohort. To estimate the total number of nursing home residents aged 60 years or more, the reported number of nursing home residents in 2010 ($n = 9236$)¹¹ was multiplied by the proportion of nursing home residents aged 60 years or more as reported by Yap et al (0.9833).

Assuming the distribution of ADL limitations among residents of nursing homes mirrors that of elderly living in the community, the number of nursing home residents in each gender and age cohort stratum was multiplied by the prevalence estimates corresponding to that stratum for 1 or 2 and 3 or more ADL limitations requiring human assistance from the SIHLS survey. In order to achieve an overall prevalence of at least 1 ADL limitation among nursing home residents equal to that reported by Yap et al (one-third of the unadjusted prevalence), the calculated number of nursing home residents with 1 or 2 and 3 or more ADL limitations in each gender and age cohort stratum was multiplied by 3 to arrive at the estimates.

Population for Simulation

In our previous research,¹² a population model for Singapore was formulated to shift cohort values (ageing in + net migration – deaths) such that individuals in a particular 1-year age cohort advance annually to the next 1-year age cohort at a single instant in time. Because these formulations introduced intra-year distortions, a revised formulation was used in this study in which chronological ages were simulated in continuous time. To do so, the members of each 1-year age cohort were advanced on every computational interval such that the length of transition was the same as the model's computational interval, which has the advantage of producing concordance with standard demographic methods.¹³ In the revised formulation, population cohorts were initialised by age and gender using Singapore Census of Population 2010 data.¹⁴ The same source was used to calculate mortality rates (based on 1-year life tables) and to estimate birth rates. In the absence of a consensus on future trends in birth and mortality rates, these parameters were held constant for all years. In addition to inflow from births, the population was simulated to increase by net migration to 6.5 million residents and expatriate workers and their families by 2050.¹⁵ However, measured migration data are not publicly available, and consequently these were estimated by comparing changes in cohort size indicated

by ageing and mortality rates obtained from published census data.²

Projection of Number of Older Adults with ADL Limitations Requiring Human Assistance

In each gender and age cohort stratum, the estimated number of nursing home residents was subtracted from the 2010 population aged ≥ 60 years, provided by the population simulation model, to arrive at the estimated community-dwelling population of older adults. The prevalence estimates for 1 or 2 and 3 or more ADL limitations from the SIHLS survey were applied to the community-dwelling population to calculate the number of community-dwelling older adults with such limitations in each stratum. In each stratum, the calculated numbers for community-dwelling older adults and older adults in nursing homes with 3 or more ADL limitations were summed. This sum was divided by the 2010 population in that stratum to provide an estimate of the prevalence of older adults with 3 or more ADL limitations requiring human assistance in the total population. A similar calculation provided an estimate of the prevalence of older adults with 1 or 2 ADL limitations requiring human assistance in the total population.

Assuming the prevalence estimates to be constant over time, the prevalence estimates were applied to the simulated population of older resident Singaporeans through 2030 to arrive at the number of resident Singaporeans aged 60 years or older with 1 or 2 and 3 or more ADL limitations requiring human assistance. Because public and private policy changes may result in a change in institutional capacity in the future, we do not provide projected numbers by place of residence of the older adults (i.e. community-dwelling or institutionalised).

Results

Table 1 presents the total population prevalence

estimates—derived by combining those for community-dwelling older adults and older adults in nursing homes—for 1 or 2 and for 3 or more ADL limitations requiring human assistance in cohorts defined by gender and age group. Figure 1 provides the estimated number of older adults in 10-year age cohorts, at five-year intervals through 2030, derived from the population model.

Table 2 applies the prevalence estimates from Table 1 to the population projection without further assumptions regarding changes in birth and mortality rates. The number of resident Singaporeans aged 60 years or older with at least 1 ADL limitation requiring human assistance is projected to increase from 31,738 in 2010 to 82,968 in 2030. Of the 82,968 Singaporeans with ADL limitations requiring human assistance, the majority are estimated to be females (69%) and to be aged 80 years or older (64%). Furthermore, while there is a slight increase in the estimated proportion of individuals with 3 or more ADL limitations requiring human assistance (52.7% in 2010 to 53.2% by 2030), the absolute number is expected to nearly triple between 2010 and 2030.

Figure 2 depicts the proportion of individuals 60 years of age and older with at least 1 ADL limitation requiring human assistance among the total population aged 60 years and older, overall and by gender. By 2030, over 7% of the population aged 60 years and older is projected to have at least 1 ADL limitation requiring human assistance.

Discussion

The results presented herein show that over the relatively short period between 2010 and 2030, the expected number of older Singaporeans with ADL limitations requiring human assistance will increase almost 3-fold. More females than males with such limitations are expected because the prevalence of ADL limitations requiring human assistance

Table 1. Estimated Prevalence of 1 or 2 and 3 or More ADL Limitations Requiring Human Assistance by Age and Gender among Population Aged at least 60 Years (Source: Data from Social Isolation Health and Lifestyles Survey and Yap et al)

Age Group	% with 1 or 2 ADL Limitations		% with 3 or More ADL Limitations	
	Female	Male	Female	Male
60 to 64	0.35	0.86	0.58	0.25
65 to 69	1.03	0.70	1.25	1.08
70 to 74	1.39	1.38	3.04	1.47
75 to 79	3.09	3.04	4.48	2.72
80 to 84	10.44	10.24	8.54	3.49
85 to 89	16.12	15.67	14.48	2.88
90 to 94	29.12	28.71	43.23	28.48
95 and older	18.73	19.39	74.93	32.92

ADL: Activity of daily living

Table 2. Estimated Older Population with ADL Limitations Requiring Human Assistance in 2010, 2020 and 2030, by Age and Gender

Year	2010			2020			2030		
	Total	Female	Male	Total	Female	Male	Total	Female	Male
Individuals with 1 or 2 ADL Limitations Requiring Human Assistance									
Age 60 to 69	2158	957	1201	3724	1697	2027	4187	2015	2172
Age 70 to 79	3246	1824	1421	5031	2776	2255	8836	4812	4024
Age 80 to 89	6698	4222	2476	10,961	6951	4009	17,548	10,931	6617
Age 90 to 99	2527	1733	794	4414	2995	1419	7089	4823	2266
Age 100 and older	378	268	110	666	493	172	1151	852	298
Total	15,006	9005	6001	24,795	14,912	9883	38,809	23,432	15,377
Individuals with 3 or More ADL Limitations Requiring Human Assistance									
Age 60 to 69	2142	1306	836	3840	2269	1570	4520	2662	1858
Age 70 to 79	4551	3175	1375	7115	4915	2200	12,161	8283	3878
Age 80 to 89	4291	3589	701	7047	5923	1124	11,177	9278	1899
Age 90 to 99	4489	3577	912	7563	5965	1599	12,385	9813	2572
Age 100 and older	1260	1073	187	2266	1973	292	3915	3408	507
Total	16,732	12,721	4011	27,831	21,046	6785	44,159	33,444	10,714
Total individuals with ADL Limitations Requiring Human Assistance									
Age 60 to 69	4300	2263	2037	7563	3966	3597	8706	4677	4030
Age 70 to 79	7796	5000	2797	12,147	7692	4455	20,997	13,095	7902
Age 80 to 89	10,988	7812	3177	18,008	12,874	5134	28,725	20,209	8516
Age 90 to 99	7016	5311	1705	11,977	8959	3018	19,474	14,636	4838
Age 100 and older	1638	1342	296	2931	2467	465	5066	4260	805
Total	31,738	21,726	10,012	52,626	35,958	16,668	82,968	56,877	26,091

ADL: Activity of daily living

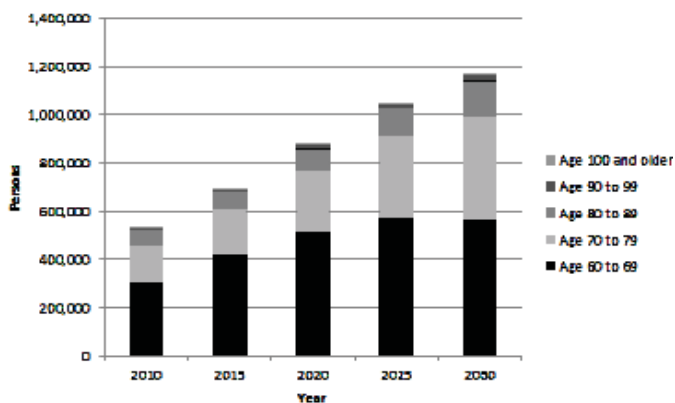


Fig. 1. Graph showing the estimated number of older adults, 2010 to 2030.

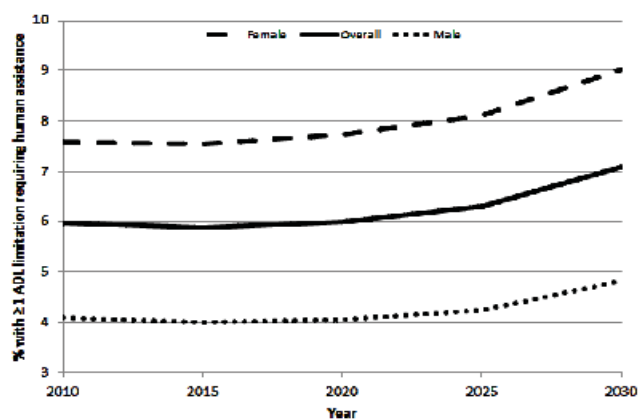


Fig. 2. Graph showing the proportion of older adults (60 years of age and older) with at least one ADL limitation requiring human assistance.

is greater in the older female population than in the male population, especially at advanced ages,¹⁶⁻¹⁸ and more females survive into old age than males.¹⁹ This gender difference in functional limitations has been reported to be due to the greater prevalence of nonfatal disabling health conditions, especially musculoskeletal conditions and depression, among females relative to males, and differences in reporting and health-related behaviours.^{16,20-22} Further, the proportion of individuals with a larger number of ADLs is expected to increase, reflecting the tendency for ADLs to accumulate with age.

As depicted in Figure 2, the simulation suggests that the proportion of individuals 60 years of age and older with at least 1 ADL limitation requiring human assistance decreases from 2010 to 2020 and then increases significantly through 2030. This reflects the fact that ADL limitations are assumed to be primarily age dependent, and that older adults aged 70 years and older are the fastest growing portion of the older population after 2020, as evident in Figure 1.

Limitations

The estimates for prevalence of ADL limitations among nursing home residents are based on a study which utilises

a convenience sample. Further representative study of nursing home residents in Singapore would improve such estimates. However, given the relatively small number of nursing home residents in Singapore (9300 in a population of over 5 million and a population aged over 65 years of approximately 303,000), modest bias in this estimate is not likely to change materially the overall estimates of numbers of individuals with ADL limitations requiring human assistance.^{23,24} The results reported consider neither the causes of ADL limitations requiring human assistance nor transition rates to more severe states. Also, the prevalence of individuals with ADL limitations requiring human assistance is assumed to remain constant. If future elderly are less impaired than the current elderly cohort, or significant improvements in technology and/or treatments are made to alleviate the need for individuals with disabling health conditions to need the assistance of others, then the projected number of individuals requiring human assistance presented herein may be an overestimate.

Conclusion

If the present ADL prevalence remains constant and population trends continue, the older Singaporean

population of 2030 (and beyond) will require more human and infrastructure resource support than the population today. Estimates of the number of older individuals with ADL limitations requiring human assistance expected over time presented in this study are of value for policymakers as well as acute and long-term care capacity planners as they seek to meet growing demands for health and social services in Singapore.

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Early Influences in Childhood Obesity—Implications for Adult Metabolic Disease

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In the past 20 years, an epidemic of adult and childhood obesity has swept through the developed world resulting in the “globesity” epidemic. This is clinically significant since obesity is a major risk factor for many chronic diseases which now occur earlier in life. Recent landmark research has identified that the intrauterine and early postnatal environment can strongly influence the risk of developing obesity and other problems in later life. The 9 months of gestation constitute the most critical period of life when the embryo miraculously develops and early life influences encountered in-utero will shape the fetus’ susceptibility to disease and its metabolism. These prenatal influences include the nutrition, drugs, chemicals and infections which the fetus was exposed to in the womb, which can significantly influence fetal development.

The pioneer of the fetal origins concept was David Barker who postulated that poor nutrition during critical periods of development can influence adult susceptibility to cardiovascular disease, type 2 diabetes mellitus and obesity.¹⁻³ The mechanism for this lies in fetal programming, which refers to the physiological adaptations leading to life-long changes in structure and function of the body. It is as though the baby receives a forecast of the nutritional environment it will encounter after birth and adapts its physiology and metabolism accordingly. This adaptation is detrimental if there is a mismatch between the predicted and actual postnatal environment.

Although the environment has been considered to be the main contributor to the obesity epidemic, the missing link between genetics and the environment is likely to found in the field of epigenetics, which has revolutionised modern biology. Epigenetics describes how the environment influences the phenotype through changes in gene expression by the addition of chemical groups to DNA which do not change the genetic code, but will change the expression of nearby genes.

Many studies on rodents have demonstrated that prenatal and postnatal environments can influence the risk of

future obesity. When rats are fed with a protein-restricted diet from conception throughout pregnancy, the offspring develop obesity with hypertension, glucose resistance and dyslipidaemia.⁴ Female rats fed an obesogenic high-fat diet before mating and peri-conceptually gave birth to obese offspring with higher blood pressure and insulin resistance compared to control offspring.⁵ In the rat model, reducing the mother’s food intake at conception and pregnancy at critical periods of development also led to persistent changes in gene expression, adversely affecting carbohydrate and lipid metabolism.^{6,7}

Early nutrition can influence DNA methylation through diet methyl donors such as choline and methionine. Rats fed a folate-deficient diet exhibited a change from normal DNA methylation to global DNA hypomethylation. Folate supplementation restored DNA methylation, which was the basis of this landmark experiment on the yellow agouti mouse.⁸ The agouti gene results in a yellow pigment, rather than the brown pigment. Maternal dietary methyl supplementation with folic acid, vitamin B12 and choline increased methylation at the agouti gene promoter and shifted the coat color distribution of the offspring towards the brown color. Interestingly, the yellow mice were more obese, more insulin resistant and developed diabetes mellitus. This is epigenetics in play as reducing methylation of the agouti gene led to obesity and insulin resistance.

The role of epigenetics in the development of human obesity is now an area of intense research, as it may provide pivotal clues to the fetal origins of obesity and the metabolic syndrome. Insights into this concept are offered through 2 historical periods of severe famine which provide a unique opportunity to study the effects of extreme dietary restriction on the population.

The Dutch Hunger Winter

The Dutch Hunger Winter lasted from November 1944 to late spring 1945 and was a bitterly cold period in Western Europe, creating extreme hardship.⁹ However, this was a

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perfectly designed but tragic experiment in nature. There were previously well-nourished women who suffered just one period of malnutrition at the same time allowing us to examine the effects of intrauterine deprivation on adult health. The study established that women exposed to famine from mid to late gestation had babies with significantly reduced birth weight. Compared to controls born before or conceived after the famine, people exposed to famine in early gestation had a more atherogenic profile, higher body mass index (BMI) and a higher risk of coronary heart disease. Those who were exposed to famine in mid or late gestation had reduced glucose tolerance with increased insulin resistance.

Heijmans et al¹⁰ subsequently discovered hypomethylation of the maternally imprinted *IGF-2* gene in individuals who were prenatally exposed to the Dutch Hunger Winter famine. Methylation of *IGF-2* silences gene expression while demethylation enables gene expression. The phenotypic consequences of hypomethylation have been implicated in the metabolic syndrome. Even more interestingly, Heijmans found that 6 decades after the famine, there was persistent hypomethylation of *IGF-2* gene in those prenatally exposed to famine as compared to unexposed same-sex siblings. Since *IGF-2* is a key factor in human growth and development, demethylation of *IGF-2* suggests that early life environmental conditions which cause epigenetic changes in humans, persist throughout life!

The Chinese famine

“The 3 years of Great Chinese Famine” from 1959 to 1961 were caused by abnormal severe drought, flooding and unwise policies of the Communist Party of China. There were an estimated 43 million famine victims. This famine lasted longer and affected more people than the Dutch Hunger winter. Li et al¹¹ established that adults who were exposed to famine during fetal life had a higher risk of metabolic syndrome as compared with non-exposed subjects, odds ratio 3.13 (95% CI, 1.24 to 7.89, $P = 0.016$). For adults exposed to famine during early childhood the odds ratio for metabolic disease was 2.85 (95% CI, 1.19 to 6.83, $P = 0.019$).

There seems to be converging data to support the hypothesis that individuals who suffered from inadequate nutrition and metabolic disturbances during fetal and postnatal development underwent incorrect ‘epigenetic programming’ and developed the metabolic syndrome. At present, there is strong evidence that environmental changes can result in the metabolic syndrome through the epidemiological studies of Barker and the famine studies which all demonstrate that early nutrition is associated with subsequent metabolic problems. From the extended Dutch Hunger Winter study, there is also evidence that

environmental changes can cause hypomethylation of the *IGF-2* gene locus. However, there is no evidence to demonstrate that these epigenetic changes directly cause the metabolic syndrome. Nonetheless, the agouti mouse model clearly demonstrates epigenetics through environment-induced gene expression causing obesity and the metabolic syndrome. Perhaps, this hypothesis may prove to be true for humans.

Deciphering the epigenetic targets and mechanisms of dysregulation by environmental exposure is the first step to translation into clinical practice. Altered epigenetic patterns may serve as biomarkers for predicting disease. They may provide new opportunities to develop prophylactic dietary strategies, akin to the use of folate for pregnant women which has reduced the spina bifida incidence. There is also the potential for the development of new drugs which can modify epigenetic changes in the form of DNA methyltransferase inhibitors and histone deacetylase inhibitors.

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A 58-year-old Woman with Dry Cough and Pulmonary Nodules

Dear Editor,

Pulmonary epithelioid haemangioendothelioma is a rare vascular neoplasm of endothelial origin. We describe a case which involved solely the lungs and a novel therapeutic strategy using pegylated liposomal doxorubicin was attempted.

Case report

A 58-year-old food-handler and life-long non-smoker presented with dry cough and exertional dyspnoea for 2 weeks duration. She had no haemoptysis, chest pain, fever, weight loss or other constitutional symptoms. Her only significant past medical history was hysterectomy with bilateral salpingoopherectomy for cervical intraepithelial neoplasia (CIN) III and endocervical adenocarcinoma-in-situ 6 years ago. Physical examination was normal.

Complete blood count, renal, hepatic panels and calcium level were all within normal ranges. Electrocardiogram and N-terminal pro brain natriuretic peptide were normal. Sputum for acid fast bacillus was negative. Her chest radiograph (CXR) and computed tomography (CT) of thorax are shown in Figure 1.

CXR showed bilateral diffuse nodular opacities (3 mm to 5 mm) and a small right pleural effusion (Fig. 1a). CT of thorax showed innumerable pulmonary nodules which appeared randomly distributed throughout both lungs (Figs. 1b and 1c). They were adjacent to bronchovascular bundles (yellow arrow 1b) and perivenular nodules (yellow arrow in Fig. 1c). They demonstrated an irregular outline and mostly measured at least 5 mm in diameter with no evidence of cavitation. Irregular thickening of bronchovascular bundles and small pleural effusions were noted bilaterally (Fig. 1d). No ground-glass change or consolidation was seen.

Bronchoscopy, bronchoalveolar lavage and transbronchial lung biopsy (TBLB) from the left lower lobe were performed. Initial hematoxylin and eosin (H&E) sections of the TBLB showed only tiny abnormal nodules of epithelioid cells in the parenchyma. Deeper sections revealed larger tumour nodules comprising epithelioid tumour cells with small nuclei/ tiny nucleoli and a small amount of eosinophilic cytoplasm; no mitotic activity was observed. They were surrounded by strands of hyaline connective tissue as highlighted by the periodic acid-Schiff diastase (PAS-D) stain. The cells did not contain mucin vacuoles. Positive immunohistochemical stains were vimentin, CD31, CD34

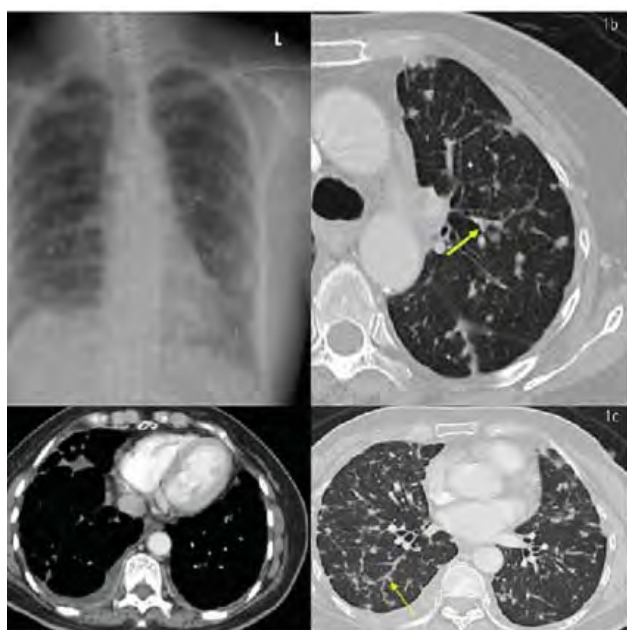


Fig. 1. Chest radiograph and computed tomography of a 58-year-old woman with dry cough and exertional dyspnoea for 2 weeks.

and Factor VIII (Von Willebrand Factor) confirming the endothelial origin of these tumour cells. The proliferation marker MIB-1 showed a low proliferative rate. Based on the biopsy and immunohistochemistry findings mentioned above, the diagnosis of pulmonary epithelioid haemangioendothelioma (PEH) was made.¹

Our patient was started on pegylated liposomal doxorubicin. She received 2 cycles of treatment and experienced clinical progression with worsening of her pleural effusion. She was then switched to sunitinib. However, she did not respond and passed away 4 months later.

Discussion

Our initial differential diagnoses based on clinical and radiological presentation were narrowed down to metastatic cancer, mycobacterial infection, sarcoidosis and less commonly diffuse pulmonary lymphangiomatosis.

Mycobacterial infection was considered but unlikely as there was no fever or other constitutional symptoms, transbronchial lung biopsy did not reveal any granulomatous inflammation and mycobacterial cultures were negative from sputum and bronchoalveolar lavage. Sarcoidosis was also deemed unlikely due to lack of hilar/mediastinal lymph node enlargement, presence of effusion (which is rare in sarcoidosis) and distribution of lung nodules (which is usually upper lobe in sarcoidosis). Diffuse pulmonary lymphangiomatosis was not considered based on age (as it is usually reported in children) and lack of lymphatic distribution of pulmonary lesions and mediastinal soft tissue infiltration.

Transbronchial lung biopsy clinched the diagnosis of pulmonary epithelioid haemangioendothelioma (PEH). It is a rare vascular neoplasm of endothelial origin with clinical behaviour intermediate between haemangioma and angiosarcoma.² It is 4 times more common in women, usually presenting between 12 and 60 years,³ as in our patient. From an internet registry,² 28% of patients were asymptomatic at presentation, and 74% of the symptomatic patients presented with chest pain. Other common symptoms are cough, haemoptysis, dyspnoea and weight loss.^{3,4} Although epithelioid haemangioendothelioma commonly involved other organs, such as liver and bone, it was not the case in our patient (Abdomen and pelvis CT did not reveal any mass, lymph node enlargement, peritoneal thickening or masses). Most cases require open lung biopsy for diagnosis but TBLB alone can diagnose PEH as supported by a previous paper.³

Adverse prognostic factors reported are male gender, age >55 years, pleural effusion or ascites,² respiratory symptoms at presentation, extensive lymphangitic spread, pleural

invasion, hepatic metastases, peripheral lymphadenopathy, fibrous pleuritis with extrapleural proliferation of tumour cells and spindle tumour cells at histology.⁴

Anthracyclines and/or ifosfamide are generally recommended in the first line treatment of patients with advanced soft tissue sarcomas (STS). Although doxorubicin is the most commonly used anthracycline in STS, treatment with this agent may be toxic at doses typically used in STS management. Hence, our patient was started on pegylated liposomal doxorubicin.⁵ She received 2 cycles of treatment and experienced clinical progression with worsening of her pleural effusion. She was then switched to sunitinib. However, she did not respond and passed away 4 months later.

In summary, this was a case of pulmonary epithelioid haemangioendothelioma that was solely diagnosed with transbronchial lung biopsy. The patient had several adverse prognostic factors and a novel therapeutic strategy was attempted but did not succeed in reversing the prognosis.

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Topical Papaverine as Rescue Therapy for Vasospasm Complicated by Unsecured Aneurysm

Dear Editor,

A 55-year-old female presented in 2010 with a World Federation of Neurosurgeons (WFNS) grade 3 subarachnoid haemorrhage (SAH). She had aneurysms of the right middle cerebral artery (MCA) (Fig. 1A) and anterior choroidal arteries, plus a left pericallosal and anterior cerebral aneurysm (ACA). Clipping was delayed by emergent Takotsubo cardiomyopathy. Coiling of the ACA aneurysm was uneventful, however the MCA aneurysm was uncoilable. Subsequent right MCA spasm was refractory to intrarterial nimodipine, and angioplasty was contraindicated given its proximity to the aneurysm (Fig. 1B). Triple-H therapy was complicated by cardiac dysfunction. Severe hemiparesis prompted urgent surgical intervention, and undiluted papaverine (120 mg/10mL) was applied directly to the spastic MCA and all other aneurysm parent vessels after clipping. We irrigated all vessels except for the right MCA with saline prior to closure. The patient responded dramatically; her hemiparesis improved significantly and transcranial Doppler showed immediate and persistent reduction in right MCA velocity from 268 cm/s to 76 cm/s.

Papaverine is usually given therapeutically at angiography, however there are reports describing instillation into the surgical bed for prophylaxis of vasospasm.¹ Intraoperative topical papaverine for the treatment of active severe vasospasm is rarely reported.² To our knowledge, this is the first such description of sustained reversal of severe symptomatic vasospasm by this method in combination with aneurysm repair in a SAH patient. The procedure is generally safe;³ reports of complications after intracisternal papaverine instillation describe severe hypotension, renal failure, bradycardia and cardiac arrest.³⁻⁵ In all 3 cases, fenestration of the lamina terminals was performed prior to the application of papaverine, which may expose the hypothalamus and/or the vagal nucleus directly to the drug.³⁻⁵ Our patient suffered no complications except for transient mydriasis. Other rare side effects reported include facial nerve palsy and monocular blindness resulting from choroidal infarction.¹ In summary, we believe this should be considered as a treatment option for similar patients, who present with unsecured aneurysms not amenable to endovascular therapy in the setting of severe vasospasm.

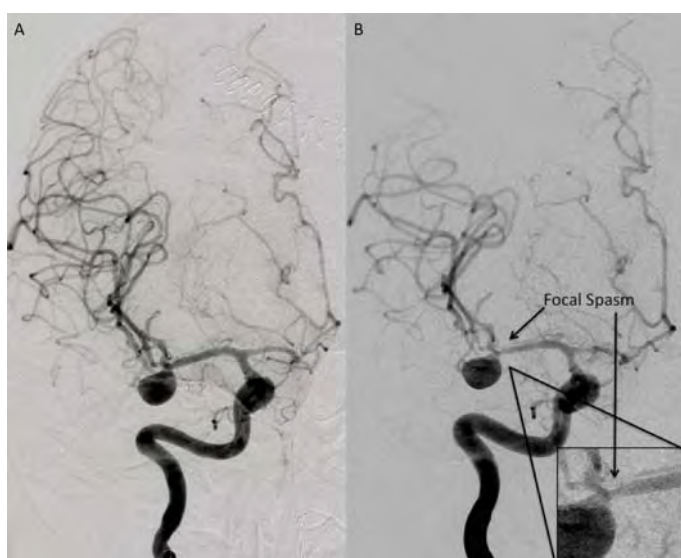


Fig. 1. Right carotid angiogram performed on days 5 (A, left) and 9 (B, right) post subarachnoid haemorrhage, showing diffuse mild middle cerebral artery spasm with a focus of more severe narrowing (arrow) immediately proximal to the large middle cerebral artery bifurcation aneurysm.

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Role of Multi-Detector Computed Tomography (MDCT) in Diagnosis of Pulmonary Artery Dissection: A Rare but Fatal Entity

Dear Editor,

A 33-year-old male who was undergoing treatment with phosphodiesterase 5 inhibitor and anticoagulant for idiopathic pulmonary arterial hypertension presented to the emergency department with acute onset of dyspnoea and chest pain. His cardiovascular examination had shown features of cardiomegaly and pulmonary arterial hypertension with no pathological murmur. His blood pressure was 138/100 mm Hg with heart rate 86 per minute. Electrocardiography showed changes suggestive of right ventricular hypertrophy with no evidence of ST segment changes. His troponin T markers for infarction were within normal limits. Chest X-ray (not shown) demonstrated cardiomegaly with biventricular enlargement. There was dilated pulmonary trunk with evidence of peripheral pruning. Patient was referred for urgent multi-detector computed tomography (MDCT) pulmonary angiography to rule out

pulmonary thromboembolism. Computed tomography (CT) pulmonary angiography was performed using 64 slice machine (GE,VCT XTE); 120 mL of contrast was administered at the rate of 4.5 mL/sec followed by 40 mL of saline at the same rate. Scanning was performed with bolus track technique with region of interest (ROI) in the right ventricle. Sections of thickness 0.625 mm were acquired. Volume rendered and contrast images were then interpreted. CT scan showed that the main and left pulmonary arteries were grossly dilated. There was evidence of intimal flap which originated just cranial to the pulmonary valve (Fig.1) and extended superiorly up to the bifurcation (Fig. 2). True and false lumens could be differentiated due to lesser enhancement and slow flow as compared to the true lumen (Fig. 3). Volume rendered (VR) images had shown grossly dilated main and left pulmonary arteries (Fig. 4). No evidence of any pulmonary thromboembolism was

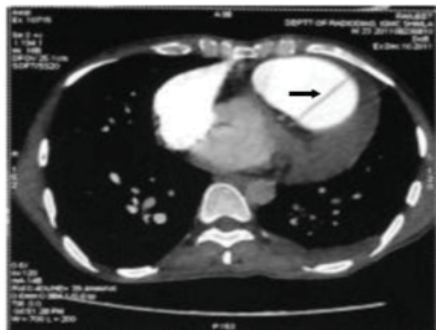


Fig. 1. Axial contrast-enhanced CT image showing intimal flap (arrow).

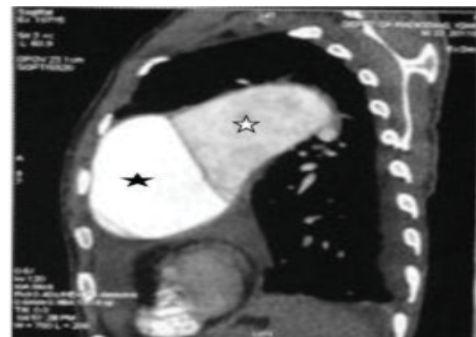


Fig. 3. Sagittal contrast-enhanced CT image showing intensely enhancing true lumen (black star) and less enhancing false lumen (white star).

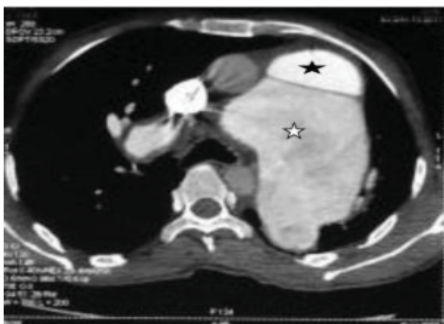


Fig. 2. Axial contrast-enhanced CT image showing true lumen (black star) and false lumen (white star) separated by intimal flap.

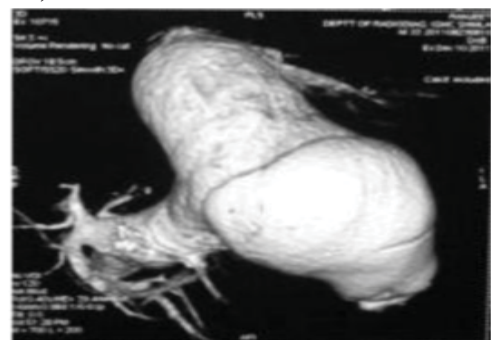


Fig. 4. Volume rendered image showing dilated main and left pulmonary arteries.

seen. The patient was managed conservatively with oxygen inhalation, beta blocker, diuretics and vasodilators. He was advised surgical intervention for which he refused.

Discussion

Pulmonary artery dissection is an extremely rare and fatal disease which is usually diagnosed on post-mortem examination.¹ It usually occurs as a complication of chronic pulmonary arterial hypertension. Other rare causes include chronic inflammation of the pulmonary arteries, right heart endocarditis, amyloidosis, trauma and severe atherosclerosis.² Although rare but in any patient with pulmonary hypertension who presents with cardiogenic shock, collapse or sudden cardiac death, diagnosis of pulmonary artery dissection should be considered as a cause.³ Often, presenting signs include dyspnoea, chest pain and cyanosis. It usually occurs at the site of maximal dilatation of pulmonary artery and had been seen related to degeneration of media on pathological studies. Reports have shown that false lumen tends to rupture rather than developing a re-entry site.⁴ Multiple modalities can be used to diagnose this entity such as echocardiography,⁵ CT,¹ Magnetic resonance imaging (MRI)⁶ and angiography.⁷ Echocardiography is usually the first-line investigation because of its ready accessibility, ease of use, and low cost. However, CT or MRI may be used if echocardiography fails to detect an intimal flap or to provide additional information related to the dissection and associated abnormalities such as pericardial tamponade.⁷ MDCT has shown many advantages over other modalities including fast volume coverage as well as isotropic resolution that allows multiplanar reformation and 3D rendering. It can accurately display the intimal flap, extent of the dissection and intraluminal thrombi. It can also demonstrate haemopericardium secondary to pulmonary artery dissection into the pericardium resulting in acute cardiac tamponade. CT can accurately evaluate the diameter and extent of the aneurysm and can exclude the presence of pulmonary embolism.¹ Isolated reports of medical management of the condition in cases where the patient had refused or was unfit for surgery are present. Although it is usually a post-mortem diagnosis but recent reports have described successful surgical repair of the dissection.⁸

Conclusion

In conclusion, we recommend that contrast-enhanced MDCT examination should be the preferred initial investigation in any patient of pulmonary hypertension to rule out this rare but fatal complication. MDCT can act as a single best modality to rule out other pathologies such as embolism, aneurismal rupture and haemopericardium.

New generation CT scanners can perform this task within seconds even in uncooperative patients.

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Blue Dye, Blue Skin

A 59-year-old Chinese lady was scheduled for wide excision of an invasive ductal carcinoma of the left breast, with sentinel lymph node biopsy (SLNB). She had a history of mild depression treated with alprazolam and paroxetine. She was assessed to be ASA (American Society of Anaesthesiologists) Class 1. Her preoperative investigative workup was normal. There was no history of atopy or prior documented drug allergy.

Standard ASA monitoring was applied. General anaesthesia was induced with midazolam, fentanyl, lignocaine, and propofol, and maintained with isoflurane in nitrous oxide and oxygen. The airway was secured with a laryngeal mask airway. Patent Blue V dye was injected in the periareolar region by the surgeon, and the sentinel lymph node was dissected. Within 10 minutes, the patient had a marked drop in arterial blood pressure to a lowest level of 69/29 mmHg, associated with tachycardia but not hypoxaemia. This was refractory to fluid resuscitation, intravenous ephedrine and phenylephrine, but responded to bolus increments of adrenaline (1.5 mg in total). Forty minutes after the onset of hypotension, the patient's skin was noted to have a bluish discolouration (Figs. 1 & 2).

What do you see in these images?

- A. Peripheral cyanosis
- B. Blue urticaria
- C. Extravasation of blue dye
- D. Methemoglobinemia
- E. Blue naevus



Fig. 1. Blue discoloration seen on the patient's abdomen.



Fig. 2. Close-up view of the well-defined blue discoloration.

Figure 1 shows blue urticaria on a background of erythema which was found over the patient's face, abdomen and limbs. Figure 2 is a close-up view of the blue urticaria—note that the blue discoloration is well demarcated and confined to the urticarial plaques.

In view of likely anaphylactic shock secondary to Patent Blue V, the patient was intubated, given intravenous hydrocortisone and diphenhydramine, and started on an intravenous adrenaline infusion for persistent hypotension. Upon urinary catheterisation, her urine was found to be blue in colour (Fig. 3). The rest of the operation was discontinued and she was transferred to the surgical intensive care unit (SICU) for monitoring and continuation of resuscitation.

The patient's serum tryptase, measured within 1 hour of the onset of hypotension, was 15.825 µg/L. The results of all other laboratory investigations were normal. She had an uneventful recovery and was discharged from the SICU the day after. Outpatient skin prick testing to confirm the allergen was offered, but declined by the patient. Since our patient did not undergo the confirmatory test, the next best management as advised by the immunologist was to avoid all putative culpable blue dyes in the future—the anaesthetic drugs per se were deemed unlikely causative agents in view of the characteristic dermatological manifestation.

Discussion

Patent Blue V is the dye of choice for intraoperative sentinel lymph node mapping for breast cancer. It belongs to the group of triphenylmethane dyes. Its ubiquitous use

Answer: B



Fig. 3. Blue urine collected upon urinary catheterisation.

as a synthetic food colouring by the general population causes sensitisation, which can lead to allergic reactions during its use in SLNB without obvious history of previous exposure. The incidence of Patent Blue V anaphylaxis is quoted to be 0.6% to 2.8%.¹

Allergic reactions to Patent Blue V can be recognised most commonly by the characteristic blue urticaria, which presents as smooth, raised patches (wheals) on a background of erythema (flare). The blue discolouration is confined to the elevated patches as the interstitial edema contains serum proteins that are bound to Patent Blue V. In more severe cases, such as in this patient, the blue urticaria can be associated with one or more of the following—angioedema, cardiovascular collapse, and respiratory distress with bronchospasm and/or laryngeal edema. Blue discolouration of urine may also be present, as in the case of this patient, and may persist for days after administration of the dye. The temporal relationship (an average of 15 to 30 minutes) between the injection of Patent Blue V and the onset of symptoms of anaphylaxis is also a guide to diagnosis.

During an intraoperative anaphylactic reaction to Patent Blue V, adrenaline, antihistamines and corticosteroids have successfully been used to restore blood pressure and resolve symptoms. Postoperative monitoring in the intensive care unit (ICU) is recommended as a second event of anaphylaxis, despite no further exposure to the allergen (biphasic anaphylaxis), has been reported.²

As anaphylaxis to Patent Blue V is a Type 1 hypersensitivity reaction, serum tryptase levels can be used to support the diagnosis of anaphylaxis. A serum tryptase level of more than 11.4 µg/L indicates systemic mast cell activation. When compared to histamine, which has a blood half-life of minutes, tryptase has a blood half-life of about 2 hours. This patient had a serum tryptase level of 15.825 µg/L. The diagnosis can be confirmed by a skin prick test where positive results may be seen at dilutions of 1:10 and 1:100 of the challenge.

To prevent the occurrence of allergic reactions, Patent Blue V product information insert recommends testing for hypersensitivity by first injecting a small volume of solution and observing for an allergic reaction prior to injection of the full volume for identification of the SLN. Safer dye alternatives such as methylene blue, with comparable efficacy for SLN identification and cost-effectiveness to that of Patent Blue V, can be considered.³

Conclusion

Collectively, the clinical symptoms (time of onset of the hypersensitivity reaction; the clinical signs and their severity) and the allergological investigations (elevated serum tryptase levels; positive skin prick test) help to determine the diagnosis of an anaphylaxis due to Patent Blue V dye.

Our case highlights the fact that blue dyes have the potential of causing life-threatening complications even after a non-systemic administration. We should remain alert for intraoperative changes that may be caused by blue dyes—hypersensitivity reactions and blue discolouration of skin and urine.

Acknowledgements

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2013 Runme Shaw Memorial Lecture: Clinical Applications of Stem Cells in Modern Medicine—21st Century and Beyond

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The rapid advancement of biomedical research in the recent years was propelled by a series of groundbreaking technological inventions and breakthrough discoveries. In this lecture, I will discuss about the scientific achievements that led to different eras of intense research with profound impact on biomedicine, focusing on the use of stem cells for research and clinical applications.

Molecular Biology Revolution

One of the most striking breakthroughs in biomedicine is the discovery of the deoxyribonucleic acid (DNA) structure by Watson and Crick. The understanding of the structure and inheritance of the genetic blueprint pioneered the molecular biology revolution. Genes were cloned, sequenced, studied and modified. It led to an unprecedented acceleration of our understanding of the gene and its products at an incredible resolution not previously known to mankind. In the molecular biology era, gene products for therapeutic uses were also manufactured. For example, the sequencing of the insulin polypeptide and the cloning of its cDNA enabled the production of large quantities of pure recombinant insulin for the treatment of diabetes. These scientific activities generated tremendous impact to the society in terms of knowledge, health and economy.

Genomics Revolution

The genetics of an individual influence different aspects of the human physiology, from physical traits to mental traits to disease susceptibility. One of the technologies that were developed in the molecular biology era is the Sanger sequencing method. Using this method, the monumental project of sequencing the human genome was completed over the course of more than 10 years. The draft of the human genome was published in 2000, and it sparked the birth of the Genomics revolution. Analysis of the correlation between genetic variants and human phenotypes has been a major research theme. Using high throughput DNA analysis approaches, genome wide association studies have led to numerous new insights into human physiology and disease.

Development of improved sequencing technologies now brings genomics research to an even higher level. Capillary-based sequencing technology was replaced by sequencing by synthesis technology, which allows for even higher throughput. More recently, single molecule-based sequencing was also developed. Today, with the current commercially available sequencing instruments, it is possible to sequence a human genome within 2 to 3 days. Concurrent with the revolution in sequencing technology, the cost of sequencing has also reduced dramatically over the past 10 years. All these developments have led to the commodification of sequencing; while in the past, only the major sequencing centers could afford a suite of sequencing instruments, the continuous drop in sequencing costs enables more deployment and application of genomics in a clinical setting. The generic way to treat patients under the assumption that everyone has equivalent response to a drug can be changed with the implementation of new genomics technologies. Advances in the Genomics era ultimately contribute to achieving the vision of Genomics Medicine / Personalised Medicine, which entails the customisation of healthcare with medical decisions, practices, and products being tailored to the genetic profile of individual patients.

Stem Cell Revolution

The global phenomenon of ageing has led to an increase in diseases associated with the elderly, many of which are due to a degeneration of physiological functions. One emerging strategy is to develop methods to replace the lost function by introducing cells or their cellular products to enhance or mediate regeneration. Arising as a promising source of these cells and cellular products for regenerative medicine are stem cells. Stem cells are undifferentiated or 'blank' cells found in the human body that are capable of perpetuating themselves as stem cells, and have the potential to develop into many different cell types that carry out various functions. Different types of stem cells have been isolated and they can be generally categorised into embryonic stem cells and tissue-specific stem cells. Tissue-specific stem cells can be isolated from the adult

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body and they can be found in a variety of different tissues such as skin, brain and liver. I would like to highlight 2 applications of tissue-specific stem cells.

One striking example is the use of stem cells to re-engineer a whole organ for transplantation to replace damaged tissues. In 2008, it was reported that a 30-year-old patient who suffered from tuberculosis had a malfunctioned airway and needed a windpipe replacement. The doctors took a donor windpipe, decellularised it and reintroduced stem cells from the patient to reconstruct the living parts of the windpipe. The windpipe graft was then transplanted back to the patient. The operation was reported to be a great success as the reconstructed windpipe was no different from the patient's own airway tissues and no signs of immune rejection were detected. The patient was able to lead a normal life up to this day. Even after years, this first tissue engineered windpipe remained functional, well vascularised and had normal ciliary function and mucus clearance. The lung function and cough reflex were also normal.¹

A second example of stem cell application is the use of cord blood stem cells for treating human diseases. In 2006, cord blood was successfully used to treat a young patient with Severe Combined Immunodeficiency which rendered the boy unable to overcome infections. After a successful cord blood transplant at the KK Women's and Children's Hospital, the patient is now in good health with a functional immune system.²

Despite these successful applications of stem cells in the clinic, most tissue-specific stem cells cannot be robustly expanded in the laboratory. Active research is ongoing to identify ways to expand tissue-specific stem cells.

On the other hand, stem cells can also be derived from early embryos. Professor James Thomson first reported the successful derivation of human embryonic stem cells from donated human blastocysts.³ These cells have several important properties. First, they can be passaged stably in the laboratory for extended periods of time. Hence, they can serve as a renewable source of cells. Second, they are pluripotent and retain the ability to differentiate into cells of the 3 major lineages (endoderm, mesoderm and ectoderm). By changing culture conditions, human ES cells can be differentiated into neurons, hepatocytes, cardiomyocytes or other cell-types. These human cells can therefore be used for biomedical research and regenerative medicine. Singapore's first step in the human embryonic stem cell arena was pioneered by the work from Professor Ariff Bongso and his team who first isolated stem cells from human preimplantation blastocysts in 1994.⁴

The biology and applications of pluripotent stem cells are spearheaded by research performed using mouse embryonic stem cells which were derived much earlier than human

embryonic stem cells. Mouse embryonic stem cells can be genetically engineered and used to create genetically modified mice, allowing for the generation of previously unavailable animal models for human diseases. Mice are now widely used as the experimental models for researchers to study gene functions *in vivo*. These groundbreaking works have led to the awarding of the Nobel Prize in Physiology or Medicine 2007 to Professors Mario R Capecchi, Sir Martin J Evans and Oliver Smithies for their discoveries of principles for introducing specific gene modifications in mice with the use of embryonic stem cells.

From the developmental biology point of view, pluripotent stem cells are also used to study early development of animals and humans. To impact clinical research, it would be necessary to derive patient-specific human embryonic stem cells. However, the derivation is technically difficult and it is also challenging due to ethical issues as human blastocysts are required.

The Birth of the “Reprogramming” Era

For a very long time, it was believed that it is not possible to convert mammalian fibroblasts, a terminally differentiated cell-type, into stem cells with a higher differentiation capacity. However, in 2006, it was demonstrated that the introduction of a simple cocktail of 4 transcription factors into mouse fibroblasts can facilitate the formation of colonies of cells that resemble mouse embryonic stem cells within 3 weeks.⁵ These cells were termed “induced pluripotent stem cells”. In 2007, there were at least 3 independent reports on the conversion of human fibroblasts into human induced pluripotent stem (iPS) cells. The technology was so straightforward that it was quickly reproduced in different laboratories worldwide. For the very first time in biology, patient-specific pluripotent stem cells can be generated easily in laboratories. This work, in conjunction with the work on demonstrating somatic cell nuclear transfer, had earned Sir John B Gurdon and Professor Shinya Yamanaka the Nobel Prize in Physiology or Medicine 2012 for the discovery that mature cells can be reprogrammed to become pluripotent.

A new field of “iPS cells” was then created. Since 2006, there are over 500 papers published on the topic. Singapore's first paper on iPS cells was published in 2009.⁶ This paper described a new combination of factors for reprogramming. In 2010, researchers from Singapore identified a new transcription factor that can improve the quality of iPS cells.⁷ The prospect of generating patient-specific iPS cells opened up many new research opportunities. It is now possible to use a patient's cells for disease modelling to investigate disease mechanisms and to screen for new or existing drugs.

Engineering the Human Genome for Gene Correction or Gene Therapy

A technology that enhances the use of stem cells for research is DNA editing. By using nucleases that recognise defined DNA sequences to mediate DNA cleavage, scientists can now effectively edit and engineer the genomic sequence of a cell. This technology encompasses the use of zinc finger, TALE and Cas9 proteins. To illustrate the potential of this technology in future medicine, I will highlight 2 examples. In the first example, zinc finger nucleases were used to direct the correction of the F9 gene to achieve a phenotypic correction of haemophilia B in a mouse model.⁸ In the second example, zinc finger nucleases were used to disrupt the CCR5 gene which encodes for the HIV co-receptor. The CD4+ T cells with mutated CCR5 gene became resistant to HIV-1 infection.⁹

What are the Major Challenges for Pluripotent Stem Cell Research?

Coupled to DNA sequencing and genome correction, the iPS cell technology allows access to individual genetics. Despite the tremendous progress in the generation of iPS cells, there are important considerations for the clinical use of these cells. First and foremost, iPS cells are not the magic bullets to all diseases. More research in the coming years would still be needed to improve our ability to differentiate pluripotent stem cells into cells that resemble the real functional cells in the body. There is also a new research frontier to generate minimal organ units from stem cells. For example, there is already good progress in transforming human embryonic stem cells into organ units such as the optic cup in the laboratory. The human embryonic stem cell-derived neural retina is able to grow into a multi-layered tissue that contains both rods and cones.¹⁰

Applications of Pluripotent Stem Cells

There are 2 major applications of pluripotent stem cells in biomedicine. First, the different cell-types that can be obtained from pluripotent stem cells can be used in drug development and human disease modelling. Cardiomyocytes derived from patient's iPS cells have been used for toxicity, safety and disease modelling studies. Cellular differences that were detected between the neurons derived from normal and Parkinson's disease patients have also enabled a better understanding of disease progression. These studies were only feasible with the development and utilisation of iPS cell technology.

The second major application of pluripotent stem cells is to use them as a source of differentiated cells for cell-based therapy. The area which is most developed is the use of retinal pigment epithelium cells for treating patients with

advanced dry age related macular degeneration or Stargardt's macular dystrophy. Safety trials are currently conducted by Advanced Cell Technology¹¹ to test the sub-retinal transplantation of retinal pigment epithelium cells derived from human embryonic stem cells. This year, the Japanese government also approved the world's first clinical trial on the use of human iPS cell-derived retinal pigment epithelium on patients with age related macular degeneration. Even though the iPS cell technology is relatively new, the stem cell field is rapidly pursuing research to advance the different applications of pluripotent stem cells in biomedicine.

Technological Advances Open up Unprecedented Opportunities for Modern Medicine

In summary, for the past 10 years, we have witnessed the development of very powerful technologies for studying the human systems which was not feasible before. The 3 major technologies are: (i) low-cost DNA sequencing, (ii) iPS cell technology, and (iii) genome editing. Today's technologies on 23 August 2013 enable the prospect of personalised genome sequencing, personalised iPS cell generation and personalised genome correction. The research done at the Genome Institute of Singapore, A*STAR, is directed towards this vision. A human genome can be sequenced within 48 hours, a human iPS cell-line can be generated within a month, and a human genome can be corrected in the laboratory within a month. While these technologies are still under development, the future prospect is exciting.

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