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"And when it rains on your parade, look up rather than down. Without the rain, there would be no rainbow."

Gilbert K Chesterton (1874 – 1936)
English writer

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Editorial

Asthma in Singapore: Past, Present and Future

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The story of asthma in Singapore over the past 50 years mirrors the history of Singapore as it progressed from a third world to a first world country.[1] In 1965, infectious diseases such as tuberculosis, diphtheria and cholera were the main challenges to public health as a consequence of poor sanitation, overcrowding and malnutrition. Asthma was not a priority. Patients often used traditional remedies ranging from herbs (Chinese, Jamu or Ayurvedic) to animal products to "cure" asthma. In 1971, a very unfortunate incident occurred. A 28- year -old asthmatic died of arsenic poisoning from taking 'Sin lak' pills, a Chinese herbal remedy for asthma. Between 1972 to 1973, two astute clinicians, Drs Tay and Seah reported an outbreak of arsenic poisoning when they observed patients with skin hyperkeratosis and areas of hyperpigmentation associated with neurological involvement and skin malignancies, occurring in asthmatics taking 'Sin Lak'.[2] 'Sin Lak' was subsequently banned in Singapore, a measure that undoubtedly saved many lives.

In that era, treatments for asthma were very diverse and included some that are no longer recommended. Private practitioners made home visits and tried to help patients with prescriptions of oral salbutamol, theophylline and steroids. Injections of subcutaneous adrenaline and intravenous aminophylline were commonly used for asthma attacks in hospitals. Inhaled corticosteroids, currently recognised as the most effective treatment for long-term control of asthma, became available in the late 1960s but were not widely accepted as the drug of choice, chiefly due to cost reasons. Asthma-related deaths were common then.

Coordination transformed this landscape. The 1980s and 1990s saw the amalgamation of dispensaries and clinics into polyclinics, which provided mass vaccination, programmes to promote health and standardised availability of drugs. Inhaled corticosteroids became more widely used and asthma mortality and admission rates fell correspondingly.[3] In 2001, the Singapore National Asthma Programme (SNAP) was launched to improve asthma control in the primary care by promoting treatment with inhaled corticosteroids and asthma education to patients. A significant shift in the drug treatment of asthma away from episodic quick relief medication towards long-term daily preventative treatment with inhaled steroids took place.[4]

By the turn of the century, Singapore had gained first world economic status and its healthcare was rated amongst the best in the world.[5] Today, inhaled preventers are easily accessible. State-of-the-art treatment such as biologics and bronchial thermoplasty are available too, where appropriate.

So, perhaps we can rest on our laurels having defeated asthma? Evidence of a disturbing rise in prevalence, magnified by gaps in awareness, and subgroups of aggressive treatment-refractory disease suggest that victory is not at hand. To elaborate, the first factor is a rising tide of "allergy epidemic" in Singapore. Eighty percent of local university students have allergen sensitisation and 18% reported asthma,[5] making Singapore one of the highest asthma prevalence communities in the world. Non-residents in Singapore develop increasing rates of sensitisation and atopy year on year when they move here,[5] suggesting that the environment in Singapore is contributing to this allergic phenomenon. Second, despite the availability of asthma medications, our asthma mortality rate is 3 times that of other developed nations such as the United States and New Zealand.[6] Sixty-seven percent of patients who had fatal or near-fatal asthma had "untreated asthma";[7] in other words, they were not receiving controller medications or regular follow-ups for asthma. In another survey of 2467 patients with asthma from 8 Asian countries which included Singapore, 73% of patients experienced 1 or more exacerbations in the past year yet 90% reported good control of asthma.[8] The mismatch between patients' perception of asthma control and the reality of outcomes (fatality, near fatal experience, exacerbations) illustrate the issues of adherence, health literacy and misinformation. Third, a small but significant proportion of asthma individuals do not respond to high-intensity, guideline-recommended treatment, and continue to have recurrent exacerbations,

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frequent hospitalisations, declining lung function and poor quality of life. These patients with severe asthma make up 5% to 10% of total asthma population but contribute to the majority of the disease-specific healthcare burden and costs. Globally, the economic costs associated with asthma have exceeded that of tuberculosis and HIV/AIDS combined.[9] The cost of asthma includes direct cost of emergency care, inpatient and outpatient services and treatment. Indirect costs include costs resulting from missed work or school (by patients and caregivers), loss of productivity or premature retirement. Developed economies can also expect increase in economic cost of asthma by >50% every 10 years.[10]

What does the future hold for asthma in Singapore? Asthma shows no sign of abating and continues to rise in Singapore aggressively. Much of what we know of asthma is derived from Western cohorts where genetics, environment, exposure and culture differ significantly from Singapore. To address this, it is necessary to marry the tools of the future with disciplined coordination and astute clinical skills.

First, we must have strong clinical research. We must collaborate to gather data and meticulously phenotype our patients.

To reduce mortality, clinicians from several restructured hospitals (Changi General Hospital, National University Hospital, Singapore General Hospital and Tan Tock Seng Hospital) have joined forces in an ongoing audit and analysis of near-fatal and fatal asthma. In parallel, there are efforts to carefully characterise the spectrum of clinical patterns of asthma patients in Singapore, ranging from the fixed airways obstruction phenotype,[11] to the frequent exacerbator phenotype,[12] atopic sensitisation patterns,[13] and adherence behaviours.[14]

Second, we must have coordinated basic science research and strong translational effort to bring useful science into clinical practice. All 3 components have to be fused by cross-discipline collaboration and public-private partnerships. Clinicians, researchers, clinician-scientists, industry and patients need to undertake a concerted effort for the collection of "omics" data (e.g. genomic, proteomic, lipidomic and microbiome) in local patient cohorts. Such efforts can lead to the identification of novel molecular endotypes or pathways of disease, generate candidate biomarkers for diagnosis, monitoring and prognostication, and identify new targets of treatment, disease modification and even cure. Provision of adequate research funding and infrastructure, coupled with the spirit of globalisation and collaboration, researchers with inquisitive mind who uphold the highest level of research ethics are all important components for a successful research programme.

Third, intelligent and coordinated use of Information Technology with Big Data and Health Services Research to perform predictive analytics for at-risk groups (e.g. children who are likely to develop problematic asthma in adulthood), high-risk groups (e.g. frequently exacerbating severe asthma) and provide information for precision medicine to individuals with special needs (e.g. biologics for severe uncontrolled asthma).

Asthma in Singapore since our independence has evolved from a low-prevalence, low-impact disease to a high-prevalence problem of significant magnitude. We are now faced with the challenges of a rising allergic epidemic, high asthma burden and high mortality but they are surmountable if we are united in our core mission to improve lives. Our pioneers have toiled to make us a world class healthcare system, so it is our turn to carry the torch and leave behind a legacy that our future generations will be proud of.

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Original Article

Awareness and Attitudes of Community-Dwelling Individuals in Singapore towards Participating in Advance Care Planning

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Abstract

Introduction: Advance care planning (ACP) is an important aspect of end-of-life care that has been shown to improve patient autonomy in decision-making and reduce stress for surviving family members. Given the rapidly ageing population in Singapore, a greater emphasis on end-of-life care planning is needed. This study therefore sought to examine the awareness and attitudes of the general Singaporean community towards participating in ACP, which are not known hitherto. Materials and Methods: A 24-item interviewer-administered questionnaire was constructed and administered via door-to-door survey amongst community-dwelling residents living in Housing and Development Board (HDB) flats across Singapore, selected via a two-stage stratified random sampling. Results: Of the 406 completed surveys, 14.4% of respondents had heard of ACP (n = 58), mostly through the media (67.9%), from family and friends (21.4%) and healthcare providers (21.4%). Only 26.8% of those who had previously heard of ACP knew how to begin an ACP discussion and 12.5% of them had a prior ACP discussion. After education, the majority of respondents were willing to begin an ACP discussion (n = 236, 60.1%). Being of an older age, having a life threatening illness, and having more knowledge about ACP were significant factors associated with willingness to have an ACP discussion. Barriers included perceiving oneself as still healthy and preferring the family to make decisions instead. Conclusion: There is a low awareness but high expressed willingness to engage in an ACP discussion amongst the Singaporean community. More efforts are needed to educate the public about ACP, engage the family unit and correct the present misconceptions.

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Key words: Advance directive, Barriers, Community, End-of-life care

Introduction

Advance care planning (ACP) involves discussions between healthcare professionals, patients and their families or carers about the patient's wishes and future healthcare plans. ACP is a significant aspect of end-of-life care that is associated with improved physical and emotional outcomes for both the patient as well as their loved ones.[1] The Agency for Integrated Care (AIC) first piloted ACP in Tan Tock Seng Hospital in 2009[2] before implementing it as a nationwide programme in 2011. Despite advocacy efforts, ACP is not widely practised in the local context.[3]

There remains a paucity of Asian studies examining the barriers and other issues related to ACP uptake, possibly because ACP was implemented only recently in the region. Besides, there are perceived cultural taboos unique to Asia regarding death. Of the few local studies available on the subject of end-of-life care, the focus was primarily on other issues such as the Advance Medical Directive (AMD).[4] This study therefore seeks to: 1) investigate the awareness of the local Singapore community towards ACP; 2) ascertain their willingness to engage in ACP discussions; and 3) identify factors that affect an individual's willingness to participate in ACP (topics that have not been studied hitherto).

Materials and Methods

In this cross-sectional study, a 24-item interviewer-administered questionnaire was developed and administered via door-to-door survey amongst community dwellers of Housing and Development Board (HDB) flats in Singapore. The residents were selected via a two-stage stratified random

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sampling within the 5 zones of Singapore, as defined by the local Urban Redevelopment Authority, namely, North, North-East, West, East and Central.[5] Surveys within each zone were conducted via a two-stage sampling design. Briefly, a list of all the residential estates in each zone was obtained and random sampling was employed to select one residential estate in each of the 5 zones. The 5 randomly-selected estates were: Sembawang (North), Punggol (North-East), Pasir Ris (East), Marine Parade (Central), and Jurong East (West). A list of all the HDB blocks located within each selected estate was then compiled and random sampling without replacement was employed to generate the order of blocks visited. Within each selected block, random sampling without replacement was employed to generate the order of floors visited. Within each floor, the household with the highest unit number was visited first, and subsequent households were visited in descending order of unit numbers.

The inclusion criteria for the study were: 1) Singapore citizen or permanent resident; 2) at least 21 years of age; 3) proficient in English or Mandarin; and 4) ability to provide informed consent.

The questionnaire was developed with reference to the current literature,[6-10] and under the guidance of domain experts in palliative medicine and public health. The questionnaire included 23 close-ended questions that evaluated the respondent's awareness and knowledge of ACP, willingness to engage in ACP, factors influencing his/her willingness to undergo an ACP discussion and demographic items (Fig. 1). If the respondent was not previously aware of ACP, or if the respondent was previously aware of ACP but had not yet begun his/her ACP discussion, an official illustration created by AIC (http://livingmatters.sg/health-care-professionals/) was used to educate him/her about ACP. The respondent's willingness to begin an ACP discussion was assessed following this. At the end of the questionnaire was a free-response question to allow additional comments regarding ACP. The questionnaire was designed to take only 10 to15 minutes to complete to avoid respondent fatigue.

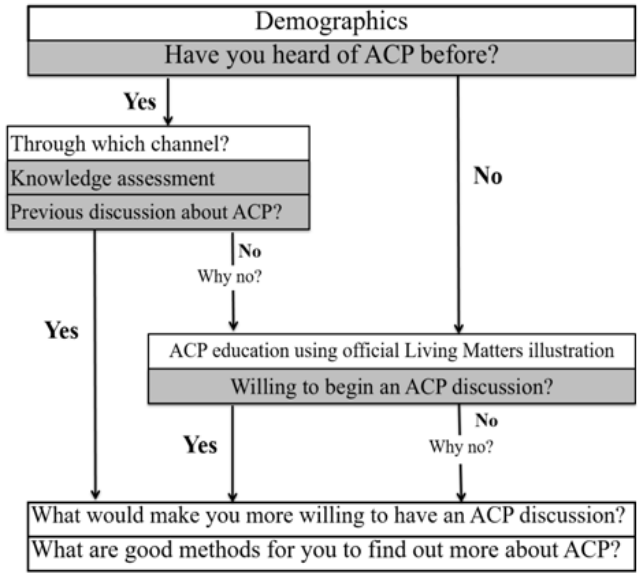

Fig. 1. Outline of the flow of questions.

The survey was administered in either English or Mandarin. The questionnaire was constructed in English and translated into Chinese, before being back-translated by an independent language teacher proficient in both languages and checked by the team for semantic equivalence. The questionnaire was also refined through pilot study with 40 random community-dwelling individuals. The aim of the pilot was to refine the wording of the questionnaires. Amendments were made based on feedback from the respondents.

Based on the results of our pilot study (17.1% awareness out of 40 random community-dwelling individuals surveyed), we postulated that the awareness of ACP in the local community was approximately 20%. A precision-based approach was then employed for sample size calculation. Adopting a 4% margin of error and assuming a 95% confidence level, an estimated sample size of 400 was anticipated.

The questionnaires were administered by 40 fourth-year medical students from the Yong Loo Lin School of Medicine, National University of Singapore (NUS). All interviewers underwent standardised interviewer training. The study protocol was approved by the local Institutional Review Board at the National University of Singapore (NUS IRB B-15-245). Verbal consent was obtained from all respondents who were provided with a participant information sheet (PIS).

All survey responses were recorded on a secure online platform. The responses were then tabulated and analysed. For continuous variables (e.g. age), the means between subgroups of interest were compared using independent sample t-tests if a normal distribution could be assumed. Means and standard deviations were reported for t-tests. Differences in proportions involving categorical variables were compared using chi-square (χ^2) tests or the Fisher's exact tests where appropriate. We summarised the association between categorical variables using frequencies and percentages, and all statistical analyses were conducted using SPSS v23.0 (IBM Corp, Armonk, NY, USA), assuming a two-sided test with 5% level of significance.

Table 1. Respondents' Demographics (n = 406)

Characteristics	Respondents*	Population Census 2010† (%)
Male, n (%)	190 (46.9)	49.3
Age (years), mean (SD)	46.8 (16.3)	
Occupation, n (%)		
Unemployed/retired	114 (28.4)	-
Employed	288 (71.6)	
Occupation, n (%)		
Non-healthcare	394 (98.0)	-
Healthcare	8 (2.0)	-
Marital status, n (%)		
Married	296 (73.1)	59.4
Single/divorced/widowed	109 (26.9)	40.6
Race, n (%)		
Chinese	273 (67.4)	74.1
Malay	64 (15.8)	13.4
Indian	53 (13.1)	9.2
Others	15 (3.7)	3.3
Nationality, n (%)		
Singapore citizen	351 (86.5)	85.7
Singapore permanent resident	55 (13.5)	14.3
Religion, n (%)		
Christianity, including Catholics	80 (19.7)	18.3
Buddhism	95 (23.4)	33.3
Taoism	28 (6.9)	10.9
Islam	71 (17.5)	14.7
Hinduism	40 (9.9)	5.1
No religion	92 (22.7)	17.0
Other religions	0 (0.0)	0.7
Religion, n (%)		
Yes	314 (77.3)	83.0
No	92 (22.7)	17.0
Highest qualification, n (%)		
Primary school and below	62 (15.3)	32.4
Secondary	86 (21.2)	18.9
Post-secondary, non-tertiary	52 (12.8)	11.1
Diploma and professional qualifications	94 (23.2)	14.8
University	112 (27.6)	22.8
Housing type, n (%)		
1-room flat or 2-room flat	21 (5.2)	4.6
3-room flat	57 (14.0)	20.0
4-room flat	189 (46.6)	31.9
5-room flat, executive flat	139 (34.2)	25.6
Condominium, landed property	0 (0.0)	16.9
Others	0 (0.0)	0.7

*Not all values tally to 406 because of responses withheld by respondents.
†Reference made to Census of Population 2010 Statistical Release 1.

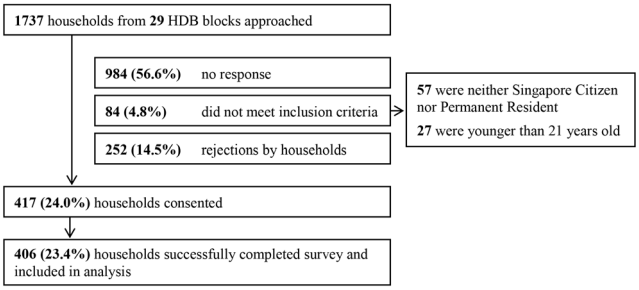

Fig. 2. Response rate.

Results

A total of 1737 household units from 29 HDB blocks were approached and the response rate is summarised in Fig. 2. The demographic attributes of our study respondents were largely similar to the population distribution of the 2010 Singapore Population Census (Table 1). A similar proportion of male and female respondents were present (46.9% and 53.1%, respectively), and the average age of our cohort was 46.8 (SD 16.2) years. Majority of our study respondents were Chinese (67.4%), followed by Malay (15.8%), Indian (13.1%) and other ethnicities (3.7%).

Awareness of the Local Singapore Community towards ACP

Fifty-eight respondents (14.4%) reported having previously heard of ACP. Respondents who were previously aware of ACP were more likely to be older (50.8 years vs 46.2 years, $P = 0.045$, $t = 2.0$, $df = 402$), Singaporean (94.8% vs 85.0%, $P = 0.043$, $\chi^2 = 4.1$, $df = 1$), and tended to make important personal decisions on their own (51.7% vs 33.0%, $P = 0.021$, $\chi^2 = 7.8$, $df = 2$) as compared to those who have not heard about ACP. Prior awareness of ACP was not associated with gender, ethnicity, occupation, marital status, nationality, religion, educational qualification, housing type, financial status and the presence of medical illness.

Majority of the individuals who have heard about ACP received the information from the media (67.9%), their family and friends (21.4%), healthcare providers (21.4%), ACP advocates (3.6%) and other sources (8.9%) such as their workplace, during a seminar and from hospital-based advertising.

These respondents were then assessed on their knowledge about ACP using 4 true-false statements (Table 2) (the 1st and 2nd statements in Table 2 are incorrect). Among the 56 individuals from whom responses were obtained for this question, 11 respondents (19.6%) answered all 4 statements correctly, while 15 respondents (26.8%) answered 3 out of 4 statements correctly, 22 respondents (39.3%) answered 2 out of 4 statements correctly, 6 respondents (10.7%) answered 1 out of 4 statements correctly and 2 respondents (3.6%) answered all 4 statements incorrectly. Notably, there was

Table 2. Respondents' Knowledge of ACP (Amongst Those Who Have Heard of ACP Previously) (n = 56)

	Respondents Correctly Identifying Statement As True/False, n (%)
ACP allows me to share my beliefs and values*	48 (85.7)
ACP is an ongoing process and I can change my decisions anytime*	41 (73.2)
ACP requires payment†	33 (58.9)
ACP is a legally binding document†	17 (30.4)

ACP: Advance care planning
*True statement.
†False statement.

Table 3. Reasons for Unwillingness to Begin an ACP Discussion (Amongst Those Who After ACP Education Were Unwilling to Begin Discussion) (n = 157)

Reason	Respondents, n (%)
I am still healthy	55 (35.0)
I find that an ACP is unnecessary	22 (14.0)
I would like my family to make the decisions for me	14 (8.9)
I still don't know enough about the ACP	13 (8.2)
I find it difficult/uncomfortable to discuss ACP topics	9 (5.7)
I do not know how to begin an ACP discussion	8 (5.1)
An ACP discussion is too troublesome	8 (5.1)
My family discourages me from making an ACP	3 (1.9)
Others	
No spare time for ACP discussion	7 (4.5)
ACP is not a priority	4 (2.5)
Unsure about usefulness since not legal binding	3 (1.9)
Believes having medical insurance is sufficient	2 (1.3)
Do not wish to discuss with an outsider	2 (1.3)
Religious and ethical considerations	2 (1.3)
Believes something similar has been done already	1 (0.6)
Missing response	4 (2.5)

ACP: Advance care planning

no association between the respondents' knowledge scores and the channels through which they had learnt about ACP.

Seven (12.5%) of these 56 respondents had a previous discussion regarding their ACP. Respondents who were more likely to have had a previous ACP discussion were those who had answered "yes" to knowing how to begin an ACP discussion (71.4% vs 20.4%, $P = 0.012$). Amongst the 49 respondents who did not have a previous ACP discussion, the top 2 reasons cited for not initiating a discussion was they still felt healthy (40.8%) and they did not know how to begin an ACP discussion (28.6%).

Willingness to Engage in ACP Discussions and Factors that Affect an Individual's Willingness to Participate in ACP

The majority of respondents (n = 348) had not previously heard of ACP before. We briefly explained ACP using a comic illustration from AIC to this group of respondents, as well as those who had previously heard of ACP but did not have a prior ACP discussion (n = 51). Of the 393 respondents who successfully received this brief education on ACP, 236 (60.1%) were willing to begin an ACP discussion post-education. Those who were willing to begin an ACP discussion were more likely to be receiving financial support from their family (40.7% vs 30.6%, $P = 0.042$, $\chi^2 = 4.1$, df = 1). There was also a trend towards those who tend to make important personal decisions together with their family (60.4% vs 48.4%, $P = 0.051$, $\chi^2 = 6.0$, df = 2) and those with university or higher education qualification (31.8% vs 21.0%, $P = 0.051$, $\chi^2 = 9.4$, df = 4) were also more likely to have greater willingness to begin an ACP discussion.

The reasons given by those who were unwilling to begin an ACP discussion are presented in Table 3. The top 3 reasons for being unwilling to begin an ACP discussion after learning more about ACP were: "I am still healthy" (35.0%), "I find that an ACP is unnecessary" (14.0%) and "I would like my family to make that decision for me" (8.9%).

All 406 respondents, regardless of whether they have heard of ACP prior to the survey, were asked what would make them more willing to have a discussion about ACP. Common factors listed by respondents were having a serious life threatening illness (83.7%), if the respondent knew more about ACP (76.8%) and if the respondent was at an older age (74.6%) (Table 4).

The top 3 methods which respondents perceived as good methods for learning more about ACP were advertisements in the media (86.9%), general practitioners or other healthcare providers advocating ACP (70.4%) and brochures given out by the government (62.6%).

Discussion

ACP may be understood as a process of health behaviour change.[7] We recognise that the survey respondents had varying levels of readiness, willingness, and different perceived barriers and benefits for participating in ACP. This suggests the utility of tailored, stage-specific interventions to improve ACP uptake. The overall low awareness and lack of knowledge regarding ACP in this study reflect a sizeable pre-contemplative population in the local community. This parallels other studies done in Australia,[8] Malaysia[9] and China[10] that have shown similar findings of low awareness of ACP in their respective populations. Evidently, more efforts should be directed towards educating the general public about ACP and its unique benefits (Fig. 3).

Table 4. Factors That Would Make Respondents More Willing to Have a Discussion About ACP (n = 406)

Option	Respondents, n (%)
If I have a serious life threatening illness	340 (83.7)
If I know more about ACP	312 (76.8)
When I'm at an older age	303 (74.6)
If the ACP is easily accessible for me to do	298 (73.4)
If my doctor talks to me about my ACP/initiates a conversation about the ACP	276 (68.0)
If I can choose who is present and who accompanies me in the discussion	266 (65.5)
If I know of someone who has done an ACP	242 (59.6)
If some financial incentives were given to me	203 (50.0)
Others	
Have more spare time for discussion	3 (0.7)
Knowledge of the benefits of ACP	3 (0.7)
Relevant anecdotal sharing	3 (0.7)
ACP is made legal	2 (0.5)
Door–to-door promotion and surveys	2 (0.5)
Doctor is willing to talk about it and is passionate	1 (0.2)
Family is supportive	1 (0.2)
Family member raises it up	1 (0.2)
Government arranges transport to attend ACP courses	1 (0.2)
More advertisement and emphasis	1 (0.2)

ACP: Advance care planning

These educational interventions should be angled towards factors that would increase one's willingness to do an ACP. As with most processes of behaviour change, while knowledge of ACP is a prerequisite for changing behaviour, it in itself is insufficient to achieve this change as motivation is a critical determinant.[11]

In this study, being of an older age (74.6%) and having a serious life threatening illness were significant motivating factors to begin an ACP discussion (83.7%). This is commonly seen in several other studies where ACP was described as unnecessary, inappropriate, premature, and unrealistic for those without a serious or life threatening disease.[12-15] Whilst it can be argued that the process of ACP is less relevant for younger and healthier individuals, in reality, life can be unpredictable and an ACP is intended to be a continuing process that will evolve over time.

Therefore, we suggest 3 platforms for public education about ACP, namely the media, healthcare professionals, and engaging the family unit.

The Media

Our study found no association between the respondents' knowledge scores and the channels through which they had learnt about ACP. This suggests that learning about ACP from the media, healthcare providers, ACP advocates, and family and friends may be equally useful. However, most of our study respondents cited media as an effective modality to learn more about ACP and most respondents who had previously heard of ACP learnt of it through the media. This finding is corroborated with a previous study in Singapore regarding knowledge of AMD, where media was found to play an important role in disseminating information about end-of-life issues.[4]

Healthcare Professionals

Majority of our respondents felt that healthcare personnel would be good channels to learn more about ACP. This finding parallels a 2012 qualitative study on 23 Korean American older adults,[12] in which most respondents preferred their physician to initiate an end-of-life discussion. However, only 22.2% of our survey respondents who had

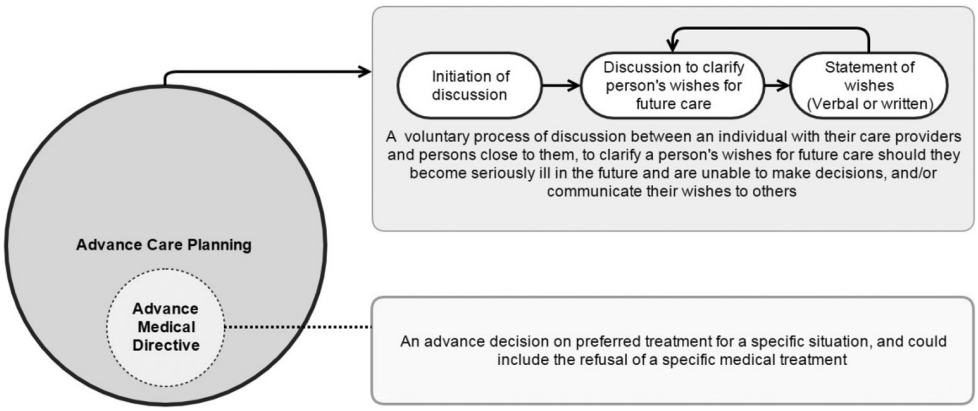

Fig. 3. Pictorial representation of advance care planning (ACP).

previously heard of ACP learnt of it through this manner. A local study conducted in 2011 found that lack of time, concerns regarding unhappiness from the family, and the perception that patients were not prepared to discuss about end-of-life preferences were barriers for physicians towards initiating an ACP discussion.[16] Another United Kingdom study in 2009 involving healthcare professionals revealed a lack of agreement as to whose responsibility it was to initiate ACP discussions and the setting in which it should be discussed.[17]

It is thus important to clarify and reaffirm the role of healthcare professionals in initiating ACP discussions, and educate them on the ACP process and the communication skills needed so they feel better equipped to discuss such matters. Individuals might not understand the clinical implications of their care and treatment preferences, and physicians are well positioned to clarify issues and provide adequate and sufficient medical or healthcare information. Timely referral to a trained ACP facilitator can also be made. ACP is akin to quality clinical encounters in medicine; physicians have a key but not an all-encompassing role.

Engaging the Family Unit

Currently in Singapore, ACP is being implemented in the majority of tertiary hospitals in selected departments, such as geriatrics or palliative care. As ACP is usually done in the presence of an individual's family members and loved ones, a potential approach would be to engage not only patients but also to extend the ACP discussion to their family members. Facilitators can utilise this opportunity to invite the patient's family members to begin ACP discussions of their own. A local study[15] found that involving the family early in ACP discussions was commonly cited as key for successful ACP. Conversely, a lack of enthusiasm from the family posed as a significant barrier to ACP discussions.

Finally, it is important to discuss the limitations of this study. Firstly, non-English and non-Mandarin speaking residents, as well as residents living in privates estates were excluded (but less than 20% of Singapore's population live in private estates[18]). Secondly, the poor participatory response in this study could be attributed to the fact that several Asian cultures, especially the Chinese, consider discussions surrounding end-of-life issues as taboo; as such, people might have refused to take part in our survey due to the taboo subject matter. Similarly, those who agreed to participate in our survey may generally be more receptive to talking about end-of-life issues than those who declined. Moreover, social desirability bias may have influenced the respondents' willingness to engage in an ACP discussion after education. This could have compromised the validity of the findings. Further studies should consider recruiting a larger number of participants from both public and private households, especially those who speak different languages. This will allow a better representation of Singapore's population and improve the validity of the results.

This is the first study of its kind specific to Singapore. A recommendation for future studies would be to validate the questionnaire used and include a qualitative component that will provide greater insight into the mindsets and attitudes of respondents. Focus group and in-depth interviews will be able to capture views not measured by our questionnaire.

Conclusion

This study found overall low awareness of ACP but high expressed willingness to engage in an ACP discussion after education. Lack of awareness of ACP is a factor contributing to current low uptake rates albeit there could be other factors. In formulating an effective approach to ACP education, possibilities include utilising media platforms, training healthcare providers on ACP administration and clarifying their role in it, and closely involving the family unit at each stage during ACP discussions.

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Original Article

Comorbid Diabetes and Depression among Older Adults – Prevalence, Correlates, Disability and Healthcare Utilisation

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Abstract

Introduction: The objectives of this current study were to: 1) examine the prevalence and correlates of diabetes mellitus (DM) among older adults (aged 60 years and above) in a multi-ethnic population; 2) examine the prevalence and correlates of comorbid DM and depression among them; and 3) assess the effect of comorbid depression on disability, cognition and healthcare utilisation. Materials and Methods: Data for the current study came from the Well-being of the Singapore Elderly (WiSE) study; a single phase, cross-sectional survey conducted among Singapore residents aged 60 years and above. A total of 2565 respondents completed the survey; depression was assessed using the Automated Geriatric Examination for Computer Assisted Taxonomy (AGECAT) while a diagnosis of DM was considered if respondents stated that a doctor had diagnosed them with DM. Results: DM was reported by 25.5% of the population. The prevalence of depression was significantly higher in those diagnosed with DM than those without DM (6% vs 3%). After adjusting for sociodemographic correlates, smoking and other chronic conditions, DM remained significantly associated with depression and subsyndromal depression. However, after including measures of functioning and cognitive impairment as covariates, DM was not significantly related to depression and subsyndromal depression. Those with comorbid DM and depression were more likely to be of Indian and Malay ethnicity, aged 75 to 84 years (versus 60 to 74 years) and widowed. Conclusion: Given the significant association of certain sociodemographic groups with comorbid depression among those with DM, targeted interventions for prevention and early diagnosis in these groups should be considered.

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Key words: Direct medical care costs, Singapore, Well-being of the Singapore elderly

Introduction

Data from studies across the world suggest that diabetes mellitus (DM) is common among those belonging to the older age group. According to a recent consensus report, the prevalence of DM among those aged ≥65 years varies from 22% to 33% in the United States (US), depending on the diagnostic criteria used.[1] Studies also suggest that depression and DM co-occur frequently.[2] A meta-analysis by Ali et al[3] found the prevalence of depression to be significantly higher in patients with type 2 DM compared with those without (17.6% vs 9.8%). Shared aetiology involving inflammatory response and dysregulation of the hypothalamic-pituitary-adrenal axis have been suggested as possible factors for this comorbidity.[4] This comorbidity leads to poorer health outcomes and increased morbidity.[5] Younger age, lower education, smoking and obesity have been associated with a higher likelihood of meeting criteria for major and minor depression among those with DM.[6]

Few studies have examined the prevalence of comorbid depression and DM among older adults in representative population samples. A study from Hong Kong based on data collected from 1998 to 2001 from elderly health centres reported that after controlling for age, sex and education level, those having regular treatment for DM were 1.3

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times more likely to have depression than older people without DM,[7] while another population-based study from Hong Kong reported that 26% of older adults with DM had elevated depressive symptoms.[8] While adjusting for self-reported disability did not attenuate this association, the association disappeared after adjusting for diabetes-related complications including heart disease, high blood pressure, stroke, and vision problems.[8] A more recent study from Brazil[9] found that 3.6% of the population aged 60 years and above had comorbid depression and DM.

Singapore is a city-state country in Southeast Asia with a population of approximately 5.5 million of which the resident population (Singapore citizens and permanent residents) totalled 3.9 million in 2015.[10] It has a multiethnic urban population comprising mainly of Chinese, Malays and Indians, each a major ethnic group in Asia. The population of older adults (defined as persons aged 65 years and older) in Singapore has grown dramatically; while in 1990 they comprised 6% of the population, this proportion has since increased to 11.8% in 2015.[11] The prevalence of type 2 DM increased from 5% in the 1980s[12] to 11% in 2010.[13] Lifetime and 12-month prevalence of major depressive disorder (MDD) in Singapore were estimated to be 5.8% and 2.2%, respectively.[14] Ethnic differences have been identified in the prevalence of both depression and DM in Singapore with Indians having the highest prevalence of DM (17.2%), followed by Malays (16.6%) and Chinese (9.7%).[13] Lifetime prevalence of MDD was also significantly higher among the Indians (8.1%) than among the Chinese (5.5%) and Malays (4.5%) in Singapore.[14] While prevalence of DM increased with age—from 1% in young adults aged 18 to 29 years to 4.3% among those aged 30 to 39 years and peaked at 29.1% among those aged 60 to 69 years[13]—the prevalence of lifetime MDD was highest in those between 18 and 34 years and lowest among those aged 65 and above.[14] However, few studies have examined comorbid depression and DM in population studies and little is known of the risk factors and consequences.

Using data from a nationwide epidemiological study among older adults in Singapore, the objectives of this current study were to: 1) examine the prevalence and correlates of DM among older adults (aged 60 years and above); 2) examine the prevalence and correlates of comorbid DM and depression in the same population; and 3) assess the effect of comorbid depression on disability, cognition and healthcare utilisation in terms of direct medical care costs.

Materials and Methods

The Well-being of the Singapore Elderly (WiSE) study was a single phase, cross-sectional survey conducted among Singapore residents (including Singapore citizens and permanent residents) aged 60 years and above. A probability sample was randomly selected from a national registry that maintains the names and sociodemographic details such as the age, gender, ethnicity and addresses of all residents in Singapore using a disproportionate stratified sampling design to obtain equivalent proportions of the 3 main ethnic groups in Singapore. In order to make inferences of prevalence rates of mental disorders to the entire Singapore resident population, the survey data were weighted to the 2011 resident population. All respondents were approached at the household; respondents who were in day care centres, nursing homes, and institutions were also included. However, those who were living outside the country and not contactable due to incomplete or incorrect addresses were excluded from the study.

The 10/66 protocol[15] was adopted for this study. The study was approved by the institutional ethics review boards of participating institutions (National Healthcare Group Domain Specific Review Board [DSRB] and the SingHealth Centralised Institutional Review Board [CIRB]). All respondents provided written informed consent and for respondents who were unable to provide informed consent, written informed consent was taken from their legally acceptable representative/next-of-kin. An "informant" was also included in the study (defined as the person who knew the respondent best). Informed consent was also obtained from all informants. The study has been described in greater detail in an earlier article.[16]

Assessment of Depression

The Geriatric Mental State (GMS) examination comprising a semi-structured interview and a rating section covering psychopathology, sensory functions and frailty was used. Diagnoses were obtained using the Automated Geriatric Examination for Computer Assisted Taxonomy (AGECAT).[17] The B3 version of the GMS generates 4 diagnostic clusters: organicity (dementia); schizophrenia and related paranoia; depression; and anxiety neurosis. A diagnostic confidence level is provided for each syndrome, ranging from 0 (no symptoms) to 5 (very severely affected). Level 3 and greater represent a degree of severity warranting professional intervention and levels 1 and 2 are classified as subcases. The validity of AGECAT has been established by Kua[18] in Singapore who reported a concordance of 0.88 (kappa) between AGECAT and the psychiatrist's diagnoses for depression. Similar to the earlier study by Guerra et al,[19] we used the stage 1 GMS-AGECAT depression syndrome for this analysis—this is subsequently referred to as "depression". Those meeting a diagnostic confidence level of 1 or 2 (subcases) were classified as "subsyndromal depression". The decision to use stage 1 diagnosis was based

on the finding that the sensitivity was consistently higher for the stage 1 than for the stage 2 depression diagnosis, against the Montgomery-Åsberg Depression Scale rating in the pilot studies.[20]

Other Assessments

Cognitive Assessment

A cognitive test battery comprising the Community Screening Interview for Dementia (CSI-D)[21] which incorporated the Consortium to Establish a Registry for Alzheimer's Dementia (CERAD) animal naming verbal fluency task, and the modified CERAD 10-word list learning task with delayed recall[22] was administered. This generated the Global Cognitive Score (COGSCORE), an item-weighted total score for cognition.

Diagnosis and Treatment of DM

Respondents were asked if a doctor had ever diagnosed them with DM. Those who reported that they had been diagnosed by a doctor as having DM were then asked if they were managed using diet alone, oral hypoglycaemics or insulin. In cases where respondents were unable to answer the query or were not sure of their answers, the "informant" was used as a proxy to collect the information.

Other Health Conditions

The presence or absence of health conditions was determined by asking respondents whether a doctor had ever told them that they had any of the following: hypertension, heart trouble (myocardial infarction, cardiac failure and valvular heart disease), stroke and transient ischaemic attacks (TIAs).

Disability

The World Health Organization Disability Assessment Schedule II (WHODAS II)[23] was used to measure limitation and participation restriction. The WHODAS II measures functioning across 6 domains – cognition, mobility, self-care, getting along, life activities and participation in community activities over the past 30 days. It uses a 5-point scale that ranges from none (0 – no difficulty) to extreme or cannot do (4 – extreme difficulty).

Resource Utilisation

Data was obtained from respondents and their informants using an adapted version of the Client Service Receipt Inventory (CSRI).[24] The instrument asks whether respondents had used specific services during the 3-month period prior to the interview. Those who endorsed receiving services were then asked in detail about the number of visits, average time spent on visits and out-of-pocket costs. Only direct medical costs were assessed for this study which included care provided by private or public setting in outpatient or inpatient setting, accident and emergency (A&E) care, as well as visits to dentists and traditional healers.

Cost of Medical Care Utilisation

Specific healthcare costs were estimated by multiplying each service unit (i.e. consultations per minute, visits per day) by their own unit cost price. For the estimation of annual costs, the 3-month values were multiplied by 4. Due to variations and paucity of data relating to unit cost from local sources, an alternative approach was used, i.e. extrapolation through application of United Kingdom (UK) unit costs was employed,[25,26] to estimate the unit cost for selected direct medical care (consultations with the primary care doctor, restructured hospital doctor, and other restructured hospital health workers). The relationship between UK and Singapore unit costs for these services were assumed to be fixed and the ratio of costs between the 2 countries to have remained unchanged over the years.[25,26] This approach consisted of the following steps: 1) determination of the reference unit costs (UK) for each specific service, 2) generation of ratios for inpatient and outpatient settings between the reference country (UK) and Singapore using data from the World Health Organisation Choosing Interventions that are Cost-Effective (WHO-CHOICE) database[27] and, 3) application of these ratios to the unit cost of each selected services in the reference country in order to generate country-specific unit costs for Singapore. The Unit Cost of Health and Social Care 2013[28] which is considered a reliable source of UK unit costs was used to identify and match the appropriate unit costs to the reported services.

This approach has been used previously in other population-based cost evaluation studies.[25,26,29,30] For other direct medical care including private healthcare doctors, other private healthcare workers, dentists, traditional healers, A&E and medication, the average out-of-pocket reported expenses amount was used instead of applying the ratios to the UK unit cost as they were deemed more representative of the Singapore population (Table 1).[26]

Body Mass Index

The weight of the respondents was measured using weighing scales after ensuring that the respondent was wearing light clothing. Height was measured by asking the respondent to stand against a wall, marking the height which was then measured using a standard tape measure.

Table 1. Unit Costs for Health and Social Services from the Societal Perspective After Conversion to Singapore Dollars

Healthcare Providers	Unit Cost (S$)	Unit of Activity	Source
Government			
Primary care (polyclinic doctor)	8.39	Minute	PSSRU 2013
Public hospital doctor	17.50	Minute	PSSRU 2013
Other public hospital healthcare worker (e.g. physiotherapist, nurse, MSWs)	1.73	Minute	PSSRU 2013
Private			
Private doctors	99.77	Visit	Out-of-pocket reported expenses (average)
Other private health workers	201.01	Visit	Out-of-pocket reported expenses (average)
Hospital admission	1069.15	Bed day	WHO-CHOICE database

MSWs: Medical social workers; PSSRU: Personal & Social Services Research Unit; WHO-CHOICE (CHOosing Interventions that are Cost-Effective)

Body mass index (BMI) was defined as the weight in kilogrammes divided by the square of the height in metres (kg/m²). WHO cutoff standards were used.[31]

Sociodemographic Information

Participants' age was established from participant report and official identification document. Information was also collected on gender, ethnicity, marital status, education, employment status, income and smoking.

Statistical Analysis

All data analyses were performed using weighted data. To ensure that the survey findings were representative of the Singapore resident elderly population, the data were weighted and analysed using survey data analysis procedures implemented in SAS version 9.2. Multiple logistic regression analyses were used to examine sociodemographic correlates of DM and comorbid DM and depression. Associations between DM and depression, comorbid DM and depression with cognition, functioning and healthcare utilisation were also examined using generalised linear models with adjustment for covariates. To account for the effects of complex sample design due to stratification and weighting,

Table 2. Descriptive Statistics of the Sample (n = 2556)

	Unweighted n	Unweighted %	Weighted %
Age group	-	-	-
60 – 74	1489	58.3	75.1
75 – 84	665	26.0	19.4
85+	402	15.7	5.6
Gender	-	-	-
Men	1111	43.5	44.0
Women	1445	56.5	56.0
Ethnicity	-	-	-
Chinese	1005	39.3	83.2
Malay	745	29.1	9.3
Indian	770	30.1	6.0
Others	36	1.4	1.5
Marital status	-	-	-
Never married	135	5.3	7.9
Married/cohabiting	1480	57.9	64.1
Widowed	832	32.6	22.4
Divorced/separated	107	4.2	5.6
Education	-	-	-
None	510	20.1	16.5
Some, but did not complete primary	618	24.3	23.9
Completed primary	638	25.1	24.8
Completed secondary	515	20.3	22.4
Completed tertiary	261	10.3	12.4
Employment status	-	-	-
Paid work (part-time and full-time)	686	27.2	34.0
Unemployed	32	1.3	1.5
Homemaker	808	32.0	26.4
Retired	1000	39.6	38.1
Received any income, benefits, pensions or allowances	-	-	-
No	371	14.5	10.7
Yes	2181	85.5	89.3
If yes, mean total monthly income (in SGD)	1998	1453.8	1631.7
Smoking	-	-	-
No	1877	73.5	74.5
Yes	676	26.5	25.5
Obesity/overweight	-	-	-
No	1203	52.8	58.0
Yes	1077	47.2	42.0
Diabetes mellitus			
No	1758	68.8	74.5
Yes	798	31.2	25.5

Table 2. Descriptive Statistics of the Sample (n = 2556) (Cont'd)

	Unweighted n	Unweighted %	Weighted %
Depression			
Depression	176	6.9	3.8
Sub-syndromal depression	422	16.5	13.3
No depression	1958	76.6	82.9
Diabetes mellitus and depression			
Comorbid diabetes mellitus and depression	72	2.8	1.5
Diabetes only	726	28.4	24.0
Depression only	104	4.1	2.2
No diabetes or depression	1654	64.7	72.3

standard errors and significance tests were estimated using the Taylor series linearisation method. Multivariate significance was evaluated using the Wald test based on design-corrected coefficient variance-covariance matrices. Statistical significance was set at the conventional level of $P < 0.05$, using two-sided tests.

Results

Prevalence, Treatment and Correlates of DM

A total of 2565 respondents completed the survey giving a response rate of 65.6%. Of these, 2556 individuals responded to the diabetes-related questions and were included in this study. Table 2 shows the descriptive statistics of the sample. The weighted percentage of those who were diagnosed by the doctor as having DM at the point of the survey was 25.5% (n = 798), of whom 79.2% (n = 623) were on oral hypoglycaemics, 12% (n = 100) were on insulin, 3% (n = 30) were managed on special diet alone, 5.1% (n = 40) were not undergoing any treatment and 0.7% (n = 5) were not sure about their treatment.

Relationship between DM and Depression

The prevalence of depression was significantly higher in those diagnosed with DM than those without DM (6% vs 3%; $P = 0.003$). After adjusting for all sociodemographic correlates, smoking and other chronic conditions, individuals with DM were more likely to be of Indian ethnicity, retired and with comorbid conditions. Additionally DM was significantly associated with depression and subsyndromal depression (Model 1, Table 3). However, after including WHODAS II and COGSCORE as a measure of disability and cognitive impairment in the covariates, DM was not significantly related to depression and subsyndromal depression (Model 2, Table 3).

Prevalence and Correlates of Comorbid DM and Depression

The prevalence of comorbid DM and depression in the overall population was 1.5% while among those with DM it was 6% (n = 72). Individuals with comorbid DM and depression as compared to those with DM alone (those with DM and comorbid subsyndromal depression were excluded from this analysis [n=155]) were more likely to be of Indian and Malay ethnicity versus Chinese ethnicity, aged 75 to 84 years (versus the younger age group) and widowed (Model 1, Table 4). After adding WHODAS II and COGSCORE in the subsequent model (Model 2, Table 4), Indian, Malay and Others ethnicity, widowed, homemakers and WHODAS scores remained significantly related to comorbid depression and DM.

Relationship between Comorbid DM and Depression with Disability, Cognition and Resource Utilisation

The mean WHODAS II score was significantly higher among those with comorbid DM and depression than those without this condition. After adjusting for all covariates, comorbid DM and depression was significantly related to WHODAS II score and total direct medical care cost (Table 5). The total annual cost of direct medical care (adjusted mean = S$14,455.64 vs S$10,310.40) including visits to a doctor in a private hospital/clinic (S$1173.86 vs S$720.59) and polyclinic (S$590.06 vs S$370.86) were significantly higher among those with comorbid DM and depression than in those with DM only.

Discussion

DM as diagnosed by a doctor was reported by 25.5% of the population. These values are slightly lower than the prevalence of 29.1% among those aged 60 to 69 years in the National Health Survey conducted in 2010.[13] The national survey included those with previously diagnosed DM as well as those diagnosed by a 2-hour glucose tolerance test which may have accounted for some of the difference. Kirkman et al[1] similarly reported that more than 25% of the US population aged ≥65 years had DM. Ethnic differences in the prevalence of DM identified in the study are similar to previous studies conducted in Singapore. The National Health Survey[13] reported that the prevalence of DM was highest among Indians and lowest among those of Chinese ethnicity. Genetic predisposition and increased insulin resistance have been suggested as putative mechanisms contributing to the increased risk of DM observed among Indians.[32] The association between DM and disability

Table 3. Sociodemographic and Clinical Correlates of Diabetes Mellitus

Demographic Characteristic	Category	Model 1†			Model 2‡		
		OR	95% CI	*P* Value	OR	95% CI	*P* Value
Age group	60 – 74	Ref.			Ref		
	75 – 84	0.9	(0.6, 1.2)	0.449	0.8	(0.6, 1.1)	0.225
	85+	0.6	(0.4, 1)	0.064	0.5	(0.3, 0.9)	0.011
Gender	Men	Ref.			Ref.		
	Women	0.7	(0.5, 1.1)	0.104	0.7	(0.5, 1)	0.083
Ethnicity	Chinese	Ref.			Ref.		
	Indian	2.3	(1.8, 3)	<0.001	2.3	(1.8, 3)	<0.001
	Malay	1.1	(0.9, 1.5)	0.383	1.1	(0.9, 1.5)	0.385
	Others	1.8	(0.9, 3.9)	0.122	1.9	(0.9, 4)	0.113
Marital status	Married	Ref.			Ref.		
	Divorced/ separated	0.9	(0.4, 1.8)	0.783	0.9	(0.4, 1.8)	0.774
	Never married	0.98	(0.5, 1.8)	0.945	0.98	(0.5, 1.8)	0.938
	Widowed	1.1	(0.8, 1.6)	0.678	1.04	(0.7, 1.5)	0.839
Education	Completed tertiary	Ref.			Ref.		
	None	1.3	(0.7, 2.4)	0.345	1.3	(0.7, 2.4)	0.337
	Some, but did not complete primary	1.1	(0.7, 1.9)	0.705	1.1	(0.7, 1.9)	0.660
	Completed primary	0.96	(0.6, 1.6)	0.871	0.98	(0.6, 1.6)	0.931
	Completed secondary	0.9	(0.5, 1.5)	0.596	0.9	(0.5, 1.5)	0.634
Employment	Paid work (part-time and full-time)	Ref.			Ref.		
	Homemaker	1.5	(0.9, 2.5)	0.085	1.5	(0.9, 2.4)	0.119
	Retired	1.7	(1.2, 2.5)	0.005	1.6	(1.1, 2.4)	0.009
	Unemployed	0.5	(0.2, 1.6)	0.248	0.5	(0.1, 1.6)	0.240
Obesity/overweight	No	Ref.			Ref.		
	Yes	1.3	(0.9, 1.7)	0.127	1.3	(0.9, 1.7)	0.128
Smoking	No	Ref.			Ref.		
	Yes	1.1	(0.8, 1.6)	0.658	1.1	(0.7, 1.5)	0.745
Depression	No depression	Ref.			Ref.		
	Cases	2.2	(1.3, 3.9)	0.005	1.7	(1, 3.1)	0.073
	Subcases	1.6	(1, 2.3)	0.028	1.4	(0.9, 2.1)	0.094
Any other chronic condition*	No	Ref.			Ref.		
	Yes	3.2	(2.3, 4.5)	<0.001	3.1	(2.2, 4.4)	<0.001
WHODAS II					1.02	(1.004, 1.03)	0.008
COGSCORE					1.02	(0.97, 1.07)	0.465

CI: Confidence interval; COGSCORE: Global Cognitive Score; OR: Odds ratio; WHODAS: World Health Organization Disability Assessment Schedule

*Includes hypertension, heart problem, heart attack, stroke and transient ischaemic attack.

†Multiple logistic regression adjusting for age, gender, ethnicity, marital status, education, employment status, obesity/overweight, smoking, depression and any other chronic condition.

‡Multiple logistic regression adjusting for age, gender, ethnicity, marital status, education, employment status, obesity/overweight, smoking, depression, any other chronic condition, COGSCORE and WHODAS II.

Table 4. Sociodemographic and Clinical Correlates of Comorbid Diabetes Mellitus and Depression[†]

Demographic Characteristic	Category	Model 1[‡]			Model 2[§]		
		OR	95% CI	*P* Value	OR	95% CI	*P* Value
Age group	60 – 74	Ref.			Ref.		
	75 – 84	2.5	(1, 6.3)	0.047	1.9	(0.6, 5.7)	0.264
	85+	1.5	(0.2, 11.7)	0.719	0.3	(0.01, 8)	0.494
Gender	Men	Ref.					
	Women	4	(0.9, 18.3)	0.078	4.7	(0.8, 27.2)	0.086
Ethnicity	Chinese	Ref.					
	Indian	4.9	(2.1, 11.3)	<0.001	6.6	(2.6, 16.5)	<0.0001
	Malay	4	(1.6, 9.8)	0.003	5.2	(1.9, 14.2)	0.001
	Others	6.6	(1, 45.5)	0.056	16.8	(3, 94.8)	0.001
Marital status	Married	Ref.					
	Divorced/separated	0.1	(0,1)	0.053	0.2	(0, 1.3)	0.096
	Never married	2.8	(0.3, 28.8)	0.396	4	(0.4, 36.5)	0.215
	Widowed	0.2	(0.1, 0.6)	0.004	0.1	(0.01, 0.4)	0.006
Education	Completed tertiary	Ref.			Ref.		
	None	2.9	(0.3, 30.2)	0.379	3.4	(0.6, 18.7)	0.167
	Some, but did not complete primary	0.6	(0.1, 5.4)	0.608	1.1	(0.2, 6.1)	0.871
	Completed primary	0.8	(0.1, 7.2)	0.806	1.3	(0.2, 8.5)	0.795
	Completed secondary	0.7	(0.1, 4.1)	0.708	0.8	(0.2, 3)	0.749
Employment	Paid work (part-time and full-time)	Ref.			Ref.		
	Homemaker	0.5	(0.1, 2.1)	0.324	0.2	(0, 1)	0.044
	Retired	0.8	(0.3, 2.2)	0.730	0.7	(0.3, 2.1)	0.540
	Unemployed	2.1	(0.2, 24.5)	0.547	2.7	(0.2, 44.8)	0.499
Obese/overweight	No	Ref.			Ref.		
	Yes	1.004	(0.4, 2.8)	0.995	1.2	(0.4, 3.4)	0.782
Smoking	No	Ref.			Ref.		
	Yes	1.9	(0.6, 6.2)	0.276	1.5	(0.4, 5.5)	0.513
Diabetes treatment	Oral hypoglycaemics	Ref.			Ref.		
	Diet alone	2.1	(0.5, 8.4)	0.274	0.99	(0.2, 4.9)	0.991
	Insulin	2.2	(0.7, 7.6)	0.192	0.8	(0.2, 3)	0.782
	No treatment	3	(0.7, 12.6)	0.143	3.3	(0.4, 25.5)	0.254
Any other chronic condition[*]	No	Ref.			Ref.		
	Yes	1.4	(0.6, 3.4)	0.448	0.7	(0.2, 2.1)	0.542
COGSCORE					1.1	(0.9, 1.2)	0.349
WHODAS II					1.1	(1.1, 1.2)	<0.0001

COGSCORE: Global Cognitive Score; WHODAS: World Health Organization Disability Assessment Schedule

[*]Any other chronic condition includes hypertension, heart problem, heart attack, stroke and transient ischaemic attack.

[†]The analysis excluded those with subsyndromal depression.

[‡]Multiple logistic regression adjusting for age, gender, ethnicity, marital status, education, employment status, obesity/overweight, smoking, diabetes treatment and any other chronic condition.

[§]Multiple logistic regression adjusting for age, gender, ethnicity, marital status, education, employment status, obesity/overweight, smoking, diabetes treatment, any other chronic condition, COGSCORE and WHODAS II.

Table 5. Relationship between Comorbid Diabetes Mellitus and Depression with Cognition, Disability and Direct Medical Care

	Comorbid Diabetes and Depression					Multivariate Regression Analyses		
	Yes (n = 72)		No (n = 571)					
	Unadjusted Mean	**SE**	**Unadjusted Mean**	**SE**	***P* Value**	**Beta Coefficient‡**	**95% CI**	***P* Value**
COGSCORE	26.98	0.79	27.94	0.27	0.844	-0.002	(-0.041, 0.036)	0.901
WHODAS II	31.64	4.80	11.94	1.07	<0.001	0.809	(0.749, 0.870)	<0.001
Annual Direct Medical Care Contacts and Costs (S$)	**Unadjusted Mean**	**SE**	**Unadjusted Mean**	**SE**	***P* Value**	**Beta Coefficient‡**	**95% CI**	***P* Value**
Primary care (polyclinic doctor)								
Number of visits	5.43	0.53	5.41	0.48	0.979	0.066	(-0.146, 0.278)	0.539
Cost	767.53	175.05	575.32	91.27	0.304	0.481	(0.940, 0.868)	0.015
Public hospital doctor*								
Number of visits	9.87	-	6.48	-	-	-	-	-
Cost	2573.88	-	2021.73	-	-			
Other public hospital health worker*								
Number of visits	5.12	-	10.8	-	-	-	-	-
Cost	120.74	-	903.8	-	-			
Private hospital/clinic doctor								
Number of visits	9.18	1.57	6.83	0.48	0.109	0.089	(-0.133, 0.311)	0.430
Cost	938.19	365.53	530.14	64.25	0.161	0.597	(0.097, 1.10)	0.020
Other private healthcare worker*								
Number of visits	18.01	-	24.41	-	-	-	-	-
Cost	2938.22	-	3348.40					
Dentist*								
Number of visits	4.00	-	7.66	-	-	-	-	-
Cost	600		4339.43					
Traditional healer								
Number of visits	21.32	-	16.69	-	-	-	-	-
Cost	1151.40	-	808.46					
Hospital admissions*								
Number of visits	41.95	-	46.16	-	-	-	-	-
Cost	48,850.26	-	49,354.56					
Emergency department/e-room†								
Cost	6065.88	-	2642.3	-	-	-	-	-
Medication								
Cost	861.33	231.40	862.33	218.92	0.997	0.073	(-0.381, 0.526)	0.754
Total direct medical care								
Cost	11,852.28	3513.16	6525.87	1357.31	0.102	0.809	(0.080, 1.538)	0.030

COGSCORE: Global Cognitive Score; WHODAS: World Health Organization Disability Assessment Schedule

*The standard error of the mean (SE), *P* values and regression coefficient were not estimated by the statistical software due to small sample size.

†The number of visits was not available in the scale.

‡Coefficient was derived using multivariate regression models after adjusting for sociodemographic factors, obesity, smoking, diabetes treatment and any chronic condition.

has been highlighted in a number of studies.[33-35] Various mechanisms including limitation in physical activity,[36,37] association with cardiovascular complications,[38] and hypoglycaemia[39] have been suggested to explain this relationship.

The study found a significant comorbidity between DM and depression, about twice what would have been expected by chance alone. These findings are similar to other reported findings in the literature.[40-41] This association was retained even after controlling for age, gender, ethnicity, education and comorbid medical conditions but it disappeared after controlling for WHODAS scores suggesting that this association may be mediated by disability.

The prevalence of comorbid DM and depression in this population and among those with DM was 1.5% and 6%, respectively. A recent systematic review[42] estimated higher prevalence rate of depression in people with type 1 (12% vs 3.2%) and type 2 DM (19.1% vs 10.7%) compared to those without. The prevalence of comorbidity is lower in our study which may be due to either methodological differences such as the use of population-based Asian sample, the inclusion of only older adults in the current study or the low prevalence of depression in this population.[43]

Other studies have identified ethnic differences in the association of depressive symptoms with DM.[44,45] Our findings of a significant association of depressive symptoms among patients with DM of Indian, Malay and Other ethnicities suggests some underlying mediating factors which may be biological, e.g. genetic,[46] psychosocial or dietary in nature. While the current study identified an association between widowhood and comorbidity, the evidence relating widowhood to poor health status and negative health behaviours is inconsistent. However, some studies have identified an association between widowhood and impairment in social functioning, depressed mood and poor physical health.[47,48]

Disability, as measured by WHODAS score, was found to be significantly associated with comorbid DM and depression. Other studies have found that the risk of diabetic complications is higher among those with DM and comorbid depression than in those with DM alone.[49] Blay et al[9] found that older adults with comorbid depression and DM were significantly more likely to have problems in their activities of daily living, and were more likely to have comorbid vascular, respiratory, urinary, and musculoskeletal disorders. Thus, comorbidity or diabetic complications may result in increased disability in the comorbid group.

Contrary to a number of other studies, we did not find an association with BMI, smoking, and education with comorbid depression and DM in the adjusted models. The study also did not find a clear pattern of higher resource utilisation among those with comorbid DM and depression. Those with comorbid depression and DM had a higher mean number of visits to doctors both in the public and private setting. They also reported more visits to traditional healers. The cost of visits to both polyclinic doctors and doctors in private setting was higher among those with comorbid DM and depression. Due to the rather small sample size of those with comorbidity, our analysis is limited. A systematic review by Hutter et al[50] similarly concluded that the number and costs of outpatient visits and total healthcare costs were increased in patients with DM and comorbid mental disorders compared with diabetic patients without such disorders. The authors further cautioned that while the increase in healthcare cost due to depression amongst those with DM may not be substantial, patients with DM already use healthcare services to a notable degree. Given this, even small to moderate increases of utilisation and cost in this group would translate into significantly increased consumption of services for healthcare providers and an increased cost burden from a policy perspective.[50]

The limitations of the study include its cross-sectional design which did not enable us to establish the temporal relation of depression and DM. There is also a possibility of under-reporting of DM and depressive symptoms among older adults which may have contributed to some of the findings. Since diagnosis of diabetes was established on the basis of self-report, we were unable to classify the type of diabetes (although we expect that the vast majority had type 2 diabetes), duration of illness or severity. Recall bias may have affected both the number of visits reported and the amount spent per visit, as the study procedures did not include checking of appointment cards or actual receipts of amount spent. The response rate of the study was about 66% and little medical data was available on those who refused to participate in the study, thus limiting the generalisability of our results to that population. Lastly, we were unable to estimate the standard error of the mean, and regression coefficient for the costs related to some of the services included in direct medical care due to the small sample size. However, the strengths include the overall large sample size, the multi-ethnic nature of the population and use of validated and structured instruments. For most of the older adults, corroborative data was also collected from an informant which reduced the probability of under-reporting by the older respondent.

Conclusion

Studies suggest that the course of DM is worsened by comorbid depression. Depression in DM has been associated with lack of self-care including failure to follow dietary restrictions and reduced physical activity,[51,52] reduced quality of life[53] and increased healthcare utilisation.[54] Thus, early

diagnosis and management of depression in patients with diabetes is essential for ensuring good outcomes. Given the significant associations of certain sociodemographic groups with comorbid depression among those with diabetes, targeted interventions for prevention and early diagnosis in these groups should be considered. For patients with comorbid depression and DM, nurse-led shared care programmes that are patient-centred and use guideline-based management of both depression and chronic disease have been shown to achieve good outcomes.[2,55]

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Original Article

Predictors and Moderators of Post-traumatic Stress Disorder: An Investigation of Anxiety Sensitivity and Resilience in Individuals with Chronic Pain

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Abstract

Introduction: Anxiety sensitivity has been proposed as a psychological vulnerability factor for post-traumatic stress disorder (PTSD). Studies have also supported the protective role of resilience for overcoming the negative effects of trauma exposure. Given the linkages between anxiety sensitivity, resilience, trauma exposure and post-traumatic stress, this study explored the potential moderating roles of anxiety sensitivity and resilience on the association between trauma history and PTSD symptoms in a sample of individuals with chronic pain. Materials and Methods: A total of 100 patients with chronic pain were recruited from a large public hospital. Patients who had pain lasting for more than 3 months and a pain intensity rating of at least 4/10 were included. The study participants were administered measures of PTSD symptoms (PTSD Checklist – Civilian Version), resilience (Brief Resilient Coping Scale) and anxiety sensitivity (Anxiety Sensitivity Index). Results: An analysis of outcome measures indicated that anxiety sensitivity and resilience were independently associated with PTSD symptoms, where βs were 0.57 and -0.23, respectively. The relationship between trauma and PTSD symptom severity was also moderated by anxiety sensitivity. Trauma history was associated with higher PTSD symptom severity only in those with high anxiety sensitivity. However, contrary to the hypotheses, resilience did not serve as a moderator. Conclusion: There are potential benefits of PTSD interventions that increase resilience and decrease anxiety sensitivity in individuals with chronic pain, especially for those who have experienced a traumatic event. Given that the presence of PTSD symptomatology in chronic pain populations negatively impact patient well-being, it would be important for clinicians to assess, monitor and treat PTSD in individuals with chronic pain.

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Key words: Singapore, Trauma exposure

Introduction

Traumatic events and the way in which people cope with them play a crucial role in the development of post-traumatic stress disorder (PTSD). Due to considerable differences in assessment strategies, sampling and other design features, there is significant variation in the prevalence of PTSD, ranging from 3% to 58%.[1,2] Chronic pain often co-occurs with PTSD, which may be due in part to the physical injuries sustained during the traumatic event or underlying physiological dysregulation associated with PTSD.[3,4] Research examining the nature of this co-occurence has found that 34% to 50% of the general population referred for the treatment of chronic pain have significant PTSD symptomatology or are diagnosed with PTSD.[3-5] The co-occurrence of these conditions is also associated with a worse prognosis with pain treatment, greater use of opioid medications and increased work and social impairment, and creates considerable personal and societal costs.[5,6]

In a focused review of research in this area, Asmundson et al found that a significant percentage of patients with chronic pain displayed PTSD symptoms, highlighting the overlap in the 2 conditions.[3] A possible link between trauma

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exposure, comorbid PTSD and chronic pain symptoms may be related to the role that anxiety sensitivity plays in both conditions. Anxiety sensitivity can be defined as the extent to which a person is sensitive to the experience of anxiety, due to their belief that the anxiety may result in negative social, psychological or physical consequences.[7,8] Anxiety sensitivity is viewed as a trait and thought to be a risk factor for the development of anxiety disorders.[9,10] Importantly, many PTSD symptoms involve arousal-related sensations (e.g. palpitations, intrusive thoughts, re-experiencing symptoms, concentration difficulties) which people with anxiety sensitivity may be particularly responsive to. As a result, individuals with an elevated level of anxiety sensitivity may be more likely than those with lower levels of anxiety sensitivity to experience the negative consequences of trauma exposure.[11,12]

Consistent with these ideas, recent studies report that anxiety sensitivity is consistently related to PTSD symptoms in trauma-exposed individuals.[13,14] Anxiety sensitivity may be relevant to PTSD symptoms in at least 2 ways: first, anxiety sensitivity may moderate or amplify symptoms following traumatic event exposure.[15-17] In other words, compared to trauma-exposed individuals with low anxiety sensitivity, those with elevated anxiety sensitivity may evaluate the initial hyperarousal sensations as more overwhelming, which may then further exacerbate such symptoms and lead to other PTSD symptoms (e.g. flashbacks).[16,17] Second, individuals with high anxiety sensitivity may be more likely to avoid reminders of a traumatic event, thereby preventing extinction of learned trauma-related fear.[18]

Based on the available research, briefly reviewed above, it is reasonable to hypothesise that people who have persistent pain with higher anxiety sensitivity may be more likely than those with lower anxiety sensitivity to report PTSD symptoms when exposed to trauma. Traumatic exposure often results in some acute stress symptoms, which may progress to PTSD or other comorbid conditions in some individuals.[19] Thus, among people who are exposed to traumatic events, individual differences in anxiety sensitivity can be viewed as a trait variable or risk factor that may demonstrate meaningful associations with post-traumatic stress symptom levels. Simply put, initial symptoms of PTSD following traumatic incidents may be worse in individuals who get overwhelmed or find bodily sensations anxiety-inducing, while other individuals who are relatively less aversive to the somatic arousal from initial symptoms of PTSD post-trauma are not likely to appraise bodily sensations as signs of illness or threat.

Traditionally, the focus of the discussion of PTSD symptoms has been on vulnerability and risk factors, including anxiety sensitivity. In recent years, the role of possible protective factors, including resilience, has been getting more consideration. Resilience was first discussed within the context of trauma and PTSD, and continues to be seen as a salutogenic factor that could potentially buffer the negative effects of trauma and PTSD.[20,21] The Brief Resilient Coping Scale (BRCS) is a measure of resilience which assesses an individual's tendencies to cope with stress in an adaptive manner.[22] It was developed on the assumption that people who endorse resilient coping behaviours are more likely to have resilient traits. It would follow that resilient traits might also be important for people with chronic pain and to understand the relationship between traumatic events and PTSD symptomatology.

In addition to its significance in the context of trauma and PTSD, the protective role of resilience had also been examined in samples of individuals with chronic health conditions. In a systematic review of 12 articles involving patients of various chronic diseases, Cal et al found that resilience was positively associated with better quality of life and negatively correlated with illness progression and psychiatric symptoms which are common among chronic illness populations.[23] The role of resilience was also studied more specifically in a sample of patients with chronic pain, where resilience was used as a framework to understand how people with chronic pain live adaptive lives.[24] Some studies using chronic pain samples have similarly found that resilience was positively associated with better adjustment in terms of pain intensity, functional impairment, anxiety and depression symptoms.[25-28] These studies illustrate the potential importance of resilience to adjustment in chronic pain populations, especially given its links to PTSD which is often comorbid with chronic pain.

There have been a number of studies demonstrating the moderating effect of resilience on the relationship between trauma exposure and PTSD symptoms. Fincham et al found that resilience moderated the relationship between childhood abuse and PTSD symptoms in adolescents, such that having greater resilience weakened the association.[29] In American veterans, while resilience was shown to attenuate the risk of PTSD diagnosis after controlling for trauma exposure, resilience also interacted with combat exposure, such that those higher in resilience evidenced weaker associations between combat exposure and a diagnosis of PTSD.[30] In a study of Korean firefighters, trauma exposure had both direct and indirect effects (through perceived stress levels) on PTSD symptomatology.[31] Comparing those who experienced similar levels of trauma exposure, firefighters with high levels of resilience were protected from both the direct and indirect impact of traumatic stress.

Studies that demonstrate the possible moderating role of resilience on the relationship between trauma exposure and PTSD symptoms have been relatively rare in chronic

pain studies. A study, conducted on women alone, found that trauma-exposed patients with chronic pain without significant PTSD symptoms had higher scores in resilience and pain acceptance than trauma-exposed patients with chronic pain who endorsed significant PTSD symptoms.[32] This suggests that not all trauma-exposed chronic pain patients would have significant PTSD symptoms, and that resilience could potentially play a role in determining whether PTSD symptoms would develop following traumatic events.

Given the linkages described above between resilience, trauma exposure and post-traumatic stress, it would be reasonable to expect that the relationship between trauma and PTSD symptoms in chronic pain populations may be moderated by resilience. To be more precise, the commonly observed positive associations between trauma and PTSD symptoms should be weakened in the presence of higher resilience. Similarly, in individuals with lower resilience, the deleterious effects of traumatic exposure may be more pronounced in the context of greater PTSD symptom severity. Having conducted a study that jointly examined the effects of resilience and anxiety sensitivity in the management of chronic pain, Ruiz-Parragá et al suggested that vulnerability variables (which includes anxiety sensitivity) and protective variables (which includes resilience) may independently affect chronic pain-related outcomes.[28] Thus, there is relevance in examining both of these factors within a single study to elucidate how these risk and protective factors may work together in the relationship between trauma exposure and its associated negative outcomes, or more specifically PTSD symptoms.

While preliminary research is supportive, additional research on the interaction of anxiety sensitivity and PTSD symptoms could help clarify the role of anxiety sensitivity as a potential vulnerability factor that contributes to the development of PTSD. We hypothesised that individuals endorsing greater anxiety sensitivity would demonstrate a stronger association between a history of trauma and severity of PTSD symptoms, while those endorsing greater resilience would demonstrate a weaker association. In addition, we examined the potential role of anxiety sensitivity and resilience as having direct effects on PTSD symptoms. We hypothesised that anxiety sensitivity and resilience would be uniquely associated with PTSD symptom severity, even when controlling for the other.

Materials and Methods

Design

This was a cross-sectional study using a convenience sample.

Participants

A total of 100 participants between the ages of 21 and 80 years, and proficient in English were recruited for this study based in Singapore. A power analysis indicated that a sample size of 100 would allow the detection of a medium effect size at a power of 93% for the hypothesised moderation effects, and a power of 94% for the hypothesised main effects.[33]

The participants were patients who reported that they had chronic low back and/or knee pain for more than 3 months, with an average pain intensity in the past week of at least 4 out of 10 (10 being the most intense). They were recruited from the National University Hospital (NUH) Orthopaedic Spine Clinic, Anaesthesia Pain Clinic and the Rheumatology Clinic through referrals. Table 1 has more details on the sample characteristics.

Demographic Information

All participants were asked to provide information regarding their age, gender, ethnicity, marital status and employment status.

Table 1. Demographic Information of Sample

Variable	Mean (SD)	No. of Participants (%)
Age (years)	48.05 (15.85)	
Gender		
Female		47 (47)
Male		53 (53)
Race		
Chinese		64 (64)
Malay		10 (10)
Indian		20 (20)
Other		6 (6)
Employment status		
Employed full-time		50 (50)
Employed part-time		6 (6)
Retired		18 (18)
Homemaker		11 (11)
Unemployed		3 (3)
Not working due to pain		12 (12)
Marital status		
Married, living together		59 (59)
Married, living separately		3 (3)
Divorced		6 (6)
Single, never married		28 (28)
Widow or widower		4 (4)
Has experienced physical, emotional and/or sexual trauma		56 (56)

SD: Standard deviation

Trauma History

Participants were asked to indicate whether they had a history of trauma by checking 1 or more of the boxes that indicated "physical", "emotional" or "sexual" trauma, or "none".

PTSD Symptoms

The PTSD Checklist – Civilian Version (PCL-C) was used to assess PTSD symptoms.[34] The 17 PCL items are based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R) criteria for PTSD. Each item describes a PTSD symptom, and respondents indicate the severity of each one in the past month on a 5-point (1 = 'Not at all' to 5 = 'Extremely') Likert scale. The PCL-C is scored by summing all responses, with higher scores indicating greater PTSD symptom severity. The scale has demonstrated excellent internal consistency (Cronbach's $\alpha = 0.97$) and test-retest reliability over a 3-day interval ($r = 0.96$).[34] It has also demonstrated convergent validity through its strong association with other PTSD measures.[34] The internal consistency (Cronbach's alpha) of the PCL-C in the current sample was 0.95, indicating excellent reliability.

Anxiety Sensitivity

We used the 16-item Anxiety Sensitivity Index (ASI) to assess anxiety sensitivity.[8] Each item is rated on a 0 ('Very little') to 4 ('Very much') scale. The ASI is scored by summing all responses, and higher scores indicate greater anxiety sensitivity. ASI demonstrates adequate test-retest reliability ($r = 0.75$ over a 2-week interval), 8 and also excellent internal consistency (Cronbach's $\alpha = 0.90$).[35] In the current sample, the ASI scores also demonstrated an excellent level of internal consistency (Cronbach's alpha = 0.94). Median-split as well as extreme scores (1 SD below mean and 1 SD above mean) have both been used in various studies to classify participants into high versus low anxiety sensitivity groups.[36-38] The median split method was chosen in the current study so that groups with sufficient sizes could be generated for analysis.

Resilience

The Brief Resilient Coping Scale (BRCS) measures an individual's tendencies to cope with stress in a resilient manner.[22] The BRCS has 4 items (e.g. "I look for creative ways to alter difficult situations"), each of which is rated on a 1 ('Not true at all') to 5 ('Very true') Likert scale. The BRCS is scored by summing all responses, with higher scores indicating greater resilience. In the scale development study, the BRCS demonstrated marginal internal consistency (Cronbach's $\alpha = 0.69$) and adequate test-retest reliability over a 6-week interval in the original scale development study ($r = 0.71$, $P < 0.001$).[22] It also exhibited convergent validity through its association with other resilience-related scales, such as measures of psychological well-being. In the current sample, the internal consistency coefficient was 0.88, indicating a good level of reliability.

Procedure

The participants were referred by doctors in the aforementioned NUH clinics for possible participation in the study if they had met the study inclusion criterion. Research assistants met potential participants and explained the study to them. If they expressed interest, written consent was obtained and the participants would complete the self-report measures. At the end of the study, each participant was thanked for his/her participation and received S$50 as a token of appreciation.

Data Analysis

We first computed means and standard deviations (continuous variables) or percentages (categorical variables) of the demographic variables for descriptive purposes. Next, we examined the associations between the demographic variables and the study criterion variables in order to determine whether (and which) demographic variables would need to be controlled in the planned regression analysis. We also evaluated the distributions of the study variables (for skewness and kurtosis) and associations among the study variables (for multicollinearity) to ensure that they met the assumptions for the analyses, as well as to understand the simple (zero-order) associations between PTSD symptoms and the factors hypothesised to be associated with PTSD symptoms. We then performed a single hierarchical multiple regression analysis to test the study hypotheses. The criterion variable was the total symptom severity score of the PCL-C. Any demographic variables that were significantly associated with the variables of interest were controlled for by entering them in Step 1. The absence/presence of traumatic event exposure was entered in Step 2. In Step 3, we entered the measures of anxiety sensitivity and resilience. Finally, in Step 4, we entered 2 interaction terms (anxiety sensitivity [centred, to minimise multicollinearity among the predictor variables] X trauma history and resilience [centred] X trauma history). In the event that 1 or both of the interaction terms made a statistically significant contribution to the prediction of PTSD symptoms, we planned to perform independent samples t-tests to examine the relationship between trauma exposure and PTSD symptoms in participants with low versus high levels on the predictor variable(s) (i.e. anxiety sensitivity or resilience) associated with the significant interaction term(s).

Results

Demographic Information of Sample

Table 1 presents the demographic information for the study sample. For the most part, the demographic variables did not correlate significantly with the study criterion variables. The only 2 exceptions were a weak association between marital status and anxiety sensitivity (r = 0.24, P <0.05) and between marital status and PTSD symptoms (r = 0.24, P <0.05). Therefore, marital status, as part of the demographic variable, was controlled by entering it in the regression analyses in the first step.

Tests for Assumptions of the Planned Regression Analyses

Table 2 presents the means and standard deviations of the study variables, as well as information about the distribution of the continuous variables. As can be seen, the skewness of the continuous variables ranged from 0.64 to 1.13 and kurtosis values ranged from 0.24 to 0.61. Therefore, the skewness and kurtosis of the 3 variables fall within the acceptable range of -2 to 2, and did not require transformation prior to use in the regression analyses.

The associations among the study variables are also presented in Table 2. The association between anxiety sensitivity and resilience was low and non-significant (r = -0.07), as was that between trauma history and resilience (r = 0.04), while the association between trauma history and anxiety sensitivity was negative and significant (r = -0.22, P <0.05). In short, the strength of the associations among the independent variables did not reach the level needed (i.e. ≥0.70) to indicate a concern that multicollinearity would bias the results.[39]

Zero Order Associations between the Study Predictors and PTSD Symptoms

Table 2 also includes the correlations between the study predictors and PTSD symptoms. Anxiety sensitivity was significantly and strongly positively correlated with total PTSD score (r = 0.63, P <0.01). Resilience was significantly and moderately negatively correlated with total PTSD score (r = -0.28, P <0.01). Exposure to traumatic events was also significantly and moderately positively correlated with total PTSD score (r = 0.35, P <0.01).

Test for Moderation Effect of Anxiety Sensitivity/Resilience

Table 3 contains the results of the regression analysis that tested the hypothesised moderation effects of anxiety sensitivity and resilience on the associations between trauma history and PTSD symptoms. Consistent with the univariate analyses, trauma exposure, high anxiety sensitivity and low resilience correlated with higher PTSD symptom severity.

Neither of the interaction terms (resilience X trauma history and anxiety sensitivity X trauma history) accounted for a statistically significant proportion of additional variance in PTSD symptoms. However, the anxiety sensitivity X trauma history situation approached statistical significance (P = 0.051), which suggested a trend worth studying further. The nature of this interaction was examined in 2 follow-up independent samples t-tests, the results of which are presented in Table 4. While trauma exposure was associated with higher PTSD symptom severity in participants with high anxiety sensitivity, trauma exposure was unrelated to PTSD symptom scores among participants with low anxiety sensitivity.

Test for Direct Effect of Anxiety Sensitivity/Resilience

Table 3 presents the findings from the regression analyses that tested the potential independent direct effects of anxiety sensitivity and resilience on PTSD symptoms. Both anxiety sensitivity and resilience were still significantly associated with PTSD symptoms even after the other variable was controlled. It should be noted that the standardised coefficient for anxiety sensitivity was greater in magnitude than that for resilience.

Table 2. Variable-related Information and Zero-Order Correlations between Variables

Variable	Mean (SD)	Skewness (SE)	Kurtosis (SE)	Zero-Order Correlations		
				1	2	3
Anxiety sensitivity	19.25 (14.04)	0.64 (0.24)	-0.24 (0.48)			
Resilience	14.45 (3.57)	-0.64 (0.24)	0.61 (0.48)	-0.07		
Trauma history	-	-	-	0.22*	-0.04	
PTSD symptoms	32.60 (14.81)	1.13 (0.24)	0.40 (0.48)	0.63‡	-0.28†	0.35‡

PTSD: Post-traumatic stress disorder; SD: Standard deviation; SE: Standard error

*P <0.05.

†P <0.01.

‡P <0.001.

Table 3. Results of Regression Analysis Predicting PCL-C Severity Scores

Step and Predictor	$R^{2§}$	$\Delta R^{2§}$	F ($\Delta R^{2§}$)	β to enter‖	t Value	VIF
Marital status	0.06	0.06	5.73*	0.24	2.39*	1.00
Trauma history	0.18	0.12	14.19‡	0.35	3.77‡	1.00
Primary study predictors	0.50	0.33	30.94‡			
Anxiety sensitivity				0.54	7.06‡	1.12
Resilience				-0.23	3.10†	1.01
Interaction terms	0.54	0.04	3.76*			
Anxiety sensitivity X trauma history				0.14	1.98	1.03
Resilience X trauma history				-0.12	1.72	1.04

PCL–C: Postraumatic Stress Disorder Checklist – Civilian Version; VIF: Variance inflation factor
*P <0.05.
†P <0.01.
‡P <0.001.
§Refers to the coefficient of multiple determination.
‖Refers to the standardised partial regression coefficient of the respective predictor.

Discussion

The results provide support for the hypothesis that anxiety sensitivity and resilience are uniquely associated with PTSD symptoms independent of the other in individuals with chronic pain. Moreover, we found a trend for the relationship between trauma and PTSD symptom severity which was moderated by anxiety sensitivity. However, contrary to the study hypotheses, resilience did not serve as a moderator in the association between trauma history and PTSD symptom severity. These findings have important theoretical and clinical implications for people with persistent pain conditions. While there is a developing literature on the relationship between anxiety sensitivity and resilience with PTSD and chronic pain, there is no extensive research literature on the role of anxiety sensitivity and resilience in PTSD level among individuals with chronic pain in Asia. This paper therefore tries to draw on what research there is as well as contribute to the body of research within an Asian population.

The positive association found between anxiety sensitivity and severity of PTSD symptoms – the higher the anxiety sensitivity, the more severe the PTSD symptoms – is consistent with previous findings.[3,16,40-45] This is unsurprising because anxiety sensitivity is a cognitive vulnerability characteristic reflecting sensitivity towards anxiety and anxiety-related sensations,[7] and many PTSD symptoms are clearly anxiety-related sensations. The negative association between resilience and PTSD symptoms found in the current study is also consistent with previous findings.[20,21] While the importance of both anxiety sensitivity and resilience has been replicated in this study, this study also shows that each variable explains the unique variance in PTSD symptoms, suggesting that anxiety sensitivity and resilience may affect PTSD symptoms through different pathways or mechanisms. In addition, the finding that the magnitude of the standardised coefficient of the relationship between anxiety sensitivity and PTSD is greater than that between resilience and PTSD suggests the possibility that anxiety sensitivity may be the more important of the 2 in predicting PTSD symptom severity in a chronic pain population.

The direct and independent effects of resilience and anxiety sensitivity on PTSD symptoms in this cross-

Table 4. Independent Samples t-Tests Comparing Relationship between PTSD Symptom Scores and Trauma History for Those with High versus Low Anxiety Sensitivity

	Trauma			No Trauma			
	n	Mean	SD	n	Mean	SD	t Value
Low anxiety sensitivity	22	26.41	8.22	26	23.04	7.54	1.48
High anxiety sensitivity	32	45.22	16.34	16	33.06	11.66	2.96†

SD: Standard deviation
*P <0.05.
†P <0.01.

sectional study cannot be regarded as evidence supporting a conclusion that both of these factors have a causal impact on PTSD symptoms. While such a finding could occur if either or both have an influence on PTSD symptoms, this finding could also occur if PTSD symptoms have a causal impact on resilience and anxiety sensitivity, or if all 3 were influenced by an additional variable or variables. An important next step is to determine whether either resilience or anxiety sensitivity has a causal impact on PTSD symptoms in people with chronic pain. This could be done, for example, through an experimental design in which resilience is increased (e.g. Thompson, Arnkoff and Glass)[46] or anxiety sensitivity is decreased (e.g. Smits, Berry, Tart and Powers)[47] and where the impact of changes in these factors on reducing PTSD symptoms is evaluated. Such research may be particularly important, given the evidence of the associations between a history of trauma and function.[48,49] Anything that can be done to help individuals improve function in the light of a trauma history would be beneficial.

The findings that anxiety sensitivity showed a trend to moderate the association between trauma exposure and PTSD symptoms in people with chronic pain – in which trauma exposure predicted greater PTSD symptom severity only in those with elevated anxiety sensitivity and not in those with low anxiety sensitivity – suggest the possibility that higher anxiety sensitivity could potentially be a vulnerability factor in the development of PTSD symptoms for those who have experienced or will experience trauma in their lives. This vulnerability factor could potentially result in greater PTSD symptom severity through amplifying PTSD symptoms and/or preventing the extinction of trauma-related fear.[16,18] However, given that this finding did not quite reach statistical significance support, there is a need for more research to closely examine this potential moderating role for anxiety sensitivity. For example, longitudinal research could be used to determine if those with higher levels of anxiety sensitivity are more prone than those with lower anxiety sensitivity to develop more PTSD symptoms over time following trauma. Such research could also examine the trajectory of fear reduction following trauma as a function of anxiety sensitivity. It also supports the potential role of research in the development of evidence-based treatments such as cognitive-behavioural therapy for anxiety sensitivity reduction,[13,39,50] in order to understand the mechanisms by which these treatments reduce anxiety sensitivity and evaluate the benefits of such treatments when provided soon after traumatic events.

In the context of chronic pain, we know that the presence of psychological dysfunction can interfere with successful treatment outcomes.[51,52] Previous preliminary research suggests that PTSD treatment alone can have a beneficial effect on individuals with chronic pain by reducing general negative mood state, decreasing avoidant behaviours, promoting emotional regulation and developing positive coping strategies.[53] These findings, especially when considered in light of the current study, suggest that the presence of PTSD symptomatology in chronic pain populations may have a significant negative impact on patient well-being. It would be important for clinicians to assess, monitor and treat PTSD when indicated in individuals with chronic pain in order to achieve the best outcomes. According to pain research, it would be expected that symptoms commonly associated with PTSD including hypervigilance,[54] sleep disruption and anxiety,[55] would worsen pain outcomes.[56] Therefore, effective treatment of these symptoms would also reduce the person's pain experience.

There are a number of important study limitations that should be considered when interpreting the results. Perhaps, most importantly (and as already mentioned), due to the cross-sectional design used by the study, causality effects (in either direction) cannot be determined. However, the findings do support the need for longitudinal and experimental research that could evaluate and establish such causal relationships, if they exist. A second limitation of the study is that we assessed trauma exposure relatively broadly (i.e. as the absence or presence of physical/emotional/sexual trauma). It is possible that stronger or more nuanced associations might have been revealed had more specific elements of the participants' trauma history (e.g. the duration of the trauma, number of traumatic events, type and severity of trauma) been assessed. It would be useful to determine in future studies, if such assessment procedures had helped to further clarify the impact of trauma and the factors that had moderated this impact. A third limitation was the reliance on participants' self-report for the assessment of all variables. This might have resulted in stronger associations among the variables (due to shared method variance) than what exist in the population. Future studies could address this issue by assessing trauma more objectively, for example, by studying groups of individuals who have recently been exposed to an objective traumatic event or by assessing the history and severity of trauma from sources other than the study participants, such as a family member who knows the participant's history. Finally, the study is also limited by its relatively small sample size. While the sample size was clearly adequate for important associations to emerge, a larger sample size may have increased the chances of detecting, for example, a moderating role for resilience.

Conclusion

In recent decades, there has been an increasing recognition that chronic pain represents much more than a simple physical or medical condition.[57] Contemporary

views and research support the importance of taking a biopsychosocial view in the understanding and treatment of chronic pain.[3] The findings from the current study are in line with this approach. We investigated the hypothesised interconnectedness between anxiety sensitivity, resilience, trauma exposure and PTSD symptoms within a clinical population with chronic pain. The results showed that anxiety sensitivity and resilience were both associated with PTSD symptom severity independent of the other. The findings also suggest the possibility that anxiety sensitivity might moderate the associations between trauma history and PTSD symptoms. The findings warrant further research to examine the potential benefits of treatments which increase resilience and decrease anxiety sensitivity in individuals with chronic pain, especially for those who have recently experienced a traumatic event.

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A Training Model for Introducing a Novel Surgical Procedure into Clinical Practice: Our Experience on Peroral Endoscopic Myotomy for Achalasia

Dear Editor,

Peroral endoscopic myotomy (POEM) is a treatment for achalasia which can potentially obviate the need for intra-abdominal surgery, whilst at the same time, deliver the same effective treatment as the current standard of care – surgical myotomy. Although POEM has shown encouraging 1-year success rates of more than 90%,[1-3] it remains a technically demanding procedure. In the absence of local experts in the field, our unit came up with a structured training programme to ensure that a new procedure can be offered safely and efficaciously. This article illustrates our journey in adopting POEM as a therapeutic procedure, including its safe introduction into clinical practice, and presents a series of our first 20 experiences with this procedure.

Materials and Methods

This was a prospective study documenting our experiences in the inception of this new modality from training until the completion of our first 20 patients who had this procedure performed on them. We obtained approval from the Institutional Review Board (IRB) for the conduct of this study.

Data collected included patient demographics as well as disease characteristics. The Eckardt[4] and dysphagia[5] scores were also obtained from patients at 1 month and 6 months after discharge. Intraoperative details including procedure duration, length of submucosal tunnelling and myotomy length were collected. Postoperatively, the patients' pain scores were collected on postoperative day 1 and on discharge. Length of hospital stay (LOS) as well as any perioperative complications were also documented. Student's paired t-test was used for statistical analysis of pre- and post-procedural comparison of Eckardt and dysphagia scores.

Training for POEM

All procedures were performed by the senior author. Training for POEM commenced 6 months before the first patient underwent the procedure. A self-structured training programme was created by our department. Initial training for the procedure was via attending a hands-on workshop which was conducted overseas. In-house training was then commenced using both explanted porcine models and live porcine models. Explanted porcine models were ordered from the local abattoir on each training session and fixed to a white box (Fig. 1). Professor Philip Chiu, who has had extensive personal experience with this procedure,[6] proctored our unit in the procedure and the necessary set-up. In total, 8 training sessions, each lasting about 4 hours, were organised prior to our first experience on patients, with 2 of these being on live porcine models.

Upon completion of animal training, we obtained the institutional approval for Implementation of New Surgical Device and Interventional Procedure for Clinical Service (NSIPC) prior to our first clinical case. The first patient was performed by the overseas expert with the series author assisting in the procedure. The subsequent 2 cases were performed by the series author, with Professor Chiu observing and mentoring in the procedure. From case 4 onwards, the series author was able to perform the procedure independently.

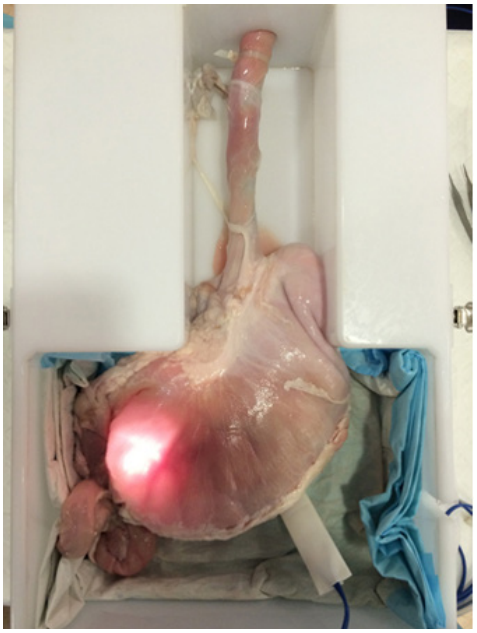

Fig. 1. Explanted porcine model, placed within a plastic box, with an endoscope in the stomach during the practice session.

Results

Our experience with POEM thus far includes 20 consecutive patients, all of which have been reported in this study. Ten of our patients were male, with a median age of 50.5 (range, 39 to 68) years. The most common complaint amongst our patients was dysphagia. Median procedural duration was 150 (79 to 294) minutes, and median length of stay was 4 (range, 1 to 50) days (Table 1).

Pain score as measured on a Visual Analogue Scale (VAS) showed a mean of 2.9 on postoperative day 1, which declined to 1.1 by the day of discharge. Out of our 20 patients, 1 suffered a myocardial infarction and required percutaneous coronary intervention. The patient was eventually discharged well. There were no other complications in this series. Patients underwent a routine gastrograffin study and gastroscopy the day after, and as all the studies did not show any leak of contrast, all patients commenced a liquid diet on post-procedure day 1.

Excluding a patient who was eventually found to have pseudoachalasia and underwent definitive total gastrectomy,

Table 1. Preoperative, Perioperative and Postoperative Findings

Patient No.	Age (Years)	Duration of Symptoms (Years)	Previous Interventions	No. of Previous Intervention(s)	Achalasia Type	Myotomy Length (cm)	Duration of Procedure (minutes)	Length of Stay (Days)	Complications
1	39	1	Balloon dilatation	1					
2	62	0.25	Nil	0					
3	44	20	Balloon dilatation	2	1	10	95	5	Nil
			Botox injection	3					
4	63	0.67	Nil	0	2	10	195	6	Nil
5	55	10	Balloon dilatation	1	3	13	122	4	Nil
6	62	45	Surgical myotomy	1	2	13	153	2	Nil
			Balloon dilataion	3					
7	52	1	Nil	0	2	14	140	4	Nil
8	53	2	Nil	0	2	13	161	4	Nil
9	33	1	Nil	0	2	15	101	1	Nil
10	51	2.5	Nil	0	2	12	94	3	Nil
11	68	30	Botox injection	1	3	15	134	2	Nil
12	67	0.875	Nil	0	3	13	150	50	ST elevation myocardial infarction
13	23	3.5	Balloon dilatation	2	1	7	218	5	Nil
			Botox injection	1					
14	34	3	Nil	0	1	10	294	5	Nil
15	33	5	Nil	0	2	14	92	2	Nil
16	38	4	Nil	0	2	14	163	3	Nil
17	49	4	Nil	0	2	14	140	3	Nil
18	50	4.5	Nil	0	3	16	214	4	Nil
19	49	10	Nil	0	1	10	192	4	Nil
20	68	15	Balloon dilatation	3	1	10	133	3	Nil

19 patients were reviewed at 1 month, and 8 at 6 months. A statistically significant decrease was noted for the Eckardt score from 5.6 to 1.3 (P <0.001) at 1 month and 0.9 (P = 0.002) at 6 months (Fig. 2). There was also a statistically significant decrease in the dysphagia score from 2.8 to 1.1 (P <0.001) at 1 month and to 1.1 (P = 0.014) at 6 months. Our intraoperative experience varied most with our initial few cases. Our third case required 258 minutes for completion largely because of difficulty in approximating the mucosal edges of the incision. We needed to use an absorbable looped suture (Loop MAJ254; Olympus, Singapore) to close the mucosal defect. In our fourth case, the distal cap attachment dislodged during the procedure and again, we used the endoscopic biopsy forceps to retrieve the cap.

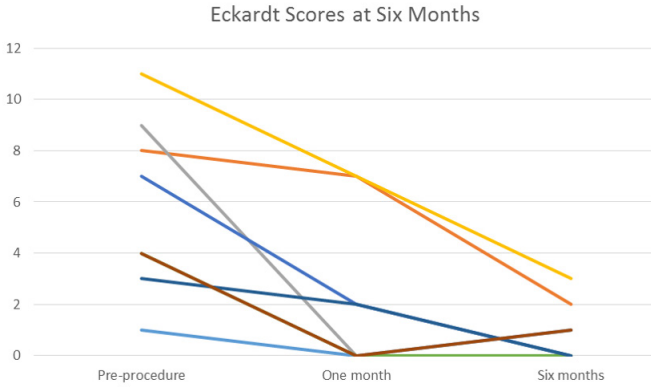

Fig. 2. Comparison of pre-, 1- and 6-months Eckardt scores. There was a statistically significant decline in the score from 5.6 to 1.3 (P <0.001) and then to 0.9 (P = 0.002).

Discussion

A structured training and proctorship programme can be implemented for new procedures with successful results. We utilised a stepwise progressive approach from attending hands-on workshop, to training on animal models and proctoring in order to bring a new procedure to our institution. Our initial results with POEM have been encouraging.

The authors believe that a comprehensive training programme is key to ensuring that the introduction of a new procedure would be safe and successful. The use of simulation-based training prior to performing a procedure in a live patient has been described in a recent review published by Dawe et al.[7] After evaluating the outcomes in both laparoscopic and endoscopic surgery, the authors concluded that there was strong evidence that preparatory simulation-based training improved overall outcomes. Bench-top training models in the form of explanted porcine models and anaesthetised animals were also suggested as suitable modes of training to reduce the learning curve in undertaking laparoscopic Roux-en-Y gastric bypass.[8]

Our training programme was designed specifically to achieve this. A two-pronged strategy was used to familiarise our unit with the procedure. We engaged the help of foreign experts through a mentorship programme on the setup and techniques in performing POEM. This was critical as POEM is a new technique in Singapore and no one else had expertise to perform this procedure. We also made use of animal models in our training, starting with porcine organs to practise on, graduating to live and anaesthetised animals. Sufficient time was also given to our unit to work as a team in performing this new procedure and to familiarise with the instruments and equipment used. We believe that this programme can be applied to the learning of other procedures and surgeries, not just for POEM.

We were able to achieve outcomes comparable to other centres globally. At 6 months, most patients achieved improvement in their symptoms. This is concordant with other large volume centres which have achieved 98% to 100% success rates.[9-11] Only 1 of our patients (5.0%) suffered a serious adverse event. Our journey in the introduction of this new procedure showed that we encountered some technical difficulties in our first few cases, as well as an incorrect diagnosis of achalasia which was only discovered after POEM was performed. In spite of these initial difficulties in the first few cases, we were able to learn from these difficulties and subsequent cases were performed smoothly.

Conclusion

A structured training programme can be implemented in a safe and effective fashion to improve the outcomes of the surgical procedures in general. Our initial experience with POEM has been encouraging and should be considered in the treatment armamentarium of achalasia.

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Too Old for Surgery? Outcomes of Hip Fracture Surgery in Centenarians

Dear Editor,

Advancement in healthcare has significantly improved overall life expectancy and it comes as no surprise that centenarians (individuals aged 100 years and above) are projected to increase by 17 fold to 3.2 million by the year 2050.[1] Ranked fourth in longest life expectancy, Singapore has already seen a 3-fold increase in 2010 to 724 centenarians just within a decade.[2,3] Since osteoporosis-related fracture risk does not diminish with advanced age, hip fracture remains a significant cause of increased morbidity and mortality in this group of patients. Management of centenarian hip fracture is especially challenging, as both healthcare providers and patients may be unwilling to consider corrective hip surgery in view of their age and perceived high anaesthetic risks. Few studies on centenarian hip fracture outcomes have been done previously and this is the first study of the centenarian population in Singapore.

Materials and Methods

Data from a single institution with an orthogeriatric co-managed hip fracture programme was acquired via a database search of admitted centenarians who had sustained new hip fractures over a 9-year period between January 2005 and December 2013. All hip fracture patients were admitted to an orthopaedic ward and were also assessed by geriatricians and anaesthesiologists with medical optimisation of heart and lung functions. Informed consent was taken for surgery and patients received either fracture fixation or hemi-arthroplasty depending on the fracture type. Postoperative rehabilitation followed an established multidisciplinary hip fracture care pathway, involving the geriatrician, physiotherapists and occupational therapists. Patients who refused surgery or were deemed unfit for surgery were managed on the conservative hip fracture care pathway, with early wheelchair mobilisation as tolerated. All patients were started on thromboembolic prophylaxis such as graduated compression stockings and mechanical calf-compression pumps.

Retrospective review of patient medical records was performed after approval from the institutional review board. Inclusion criteria was centenarians with confirmed radiological diagnosis of a hip fractures (femoral neck, intertrochanteric or subtrochanteric type) and they were followed up for at least 1 year after discharge. Patients with active oncological history or severe concomitant injuries were excluded from the study.

At the conclusion of review in October 2014, patients who were deceased were confirmed via records taken from the death registry. Detailed analysis of the complete medical records of all patients in the study cohort was performed to understand individual patient profiles, including using the Charlson Comorbidity Index (CCI [a scoring system that ranges from 0 to 33, with diseases carrying different weightage in estimating risk of death of patients from comorbidity]).[4] The higher the CCI score, the greater the mortality risk within a 1-year period.

Statistical analysis was carried out using the Statistical Package for the Social Sciences programme. Mean and standard deviations were calculated, and comparisons were made via the one-way analysis of variance (ANOVA) test, with P values of <0.05 considered as statistically significant.

Results

Patient Profile and Comorbidities

Patient demographics are as shown in Table 1 and 2, comprising 13 patients (10 women, 3 men) with a mean age of 102.3 years (range, 100.1 years to 109.8 years), with no excluded patients. Majority were Chinese (92.2%) and each patient sustained only 1 hip fracture after his or her hundredth birthday. Patients were categorised into 2 groups based on the orthopaedic management operative group (Group A) and non-operative group (Group B).

Table 1. Patient Demographics and Profile

Parameters	Operative Group A (n = 6)	Conservative Group B (n = 7)
Mean age	101.9 years (range, 100.1– 107.1)	102.8 years (range, 100.1– 109.7)
Premorbid ambulation status	All ambulant (5 require aids)	4 ambulant (2 require aids) 3 chair or bedbound
Mean ASA score	III (range, II to IIIE)	I and III*
Mean CCI	1 (range, 0 – 2)	1.29 (range 0 – 3)
Anaemia†	83.3%	85.7%

ASA: American Society of Anesthesia score; CCI: Charlson Comorbidity Index

*Unrecorded in 5 patients.

†Anemia taken as <12.0g/dL for female, <13.5g/dL for male.

Table 2. Treatment, Function Status and Mortality of Individual Patient

No.	Age	Fracture Type	Treatment	ASA	CCI	Mortality within 1 Year	Time from Injury to Death (Days)	Previous Ambulatory Status	Latest Ambulatory Status	Length of Stay (Days)
1	101y 4m	IT	PFNA	III	2	No	-	AID	AID	8
2	100y 2m†	IT	PFNA	II	0	No	-	AID	AID	24
3	107y 2m	IT	PFNA	III	0	No	-	AID	AID	20
4	102y 4m	NOF	Hemi-arthroplasty	IIE	2	Yes	97	AMB	AID	9
5	100y 4m	IT	DHS*	IIIE	1	No	1079	AMB	AMB	11
6	100y 5m	IT	PFNA	III	1	Yes	205	AID	Non-AMB	13
7	109y 9m‡	NOF	Non-OP	I	1	Yes	9	Non-AMB	Non-AMB	6
8	100y 4m†	IT	Non-OP	III	1	Yes	237	AMB	Non-AMB	9
9	100y 2m‡	NOF	Non-OP	NR	1	No	-	Non-AMB	Non-AMB	16
10	101y 10m‡	ST	Non-OP	NR	2	Yes	157	Non-AMB	Non-AMB	5
11	104y 1m	NOF	Non-OP	NR	3	No	-	AID	Non-AMB	6
12	102y 5m†	NOF	Non-OP	NR	1	Yes	62	AMB	Non-AMB	21
13	100y 8m	NOF	Non-OP	NR	0	No	-	AID	AID	9

AID: Ambulant with walking aid; AMB: Ambulant without walking aid; ASA: American Society of Anesthesia score; CCI: Charlson Comorbidity Index; DHS: Dynamic hip screw; IT: Intertrochanteric; NOF: Neck of femur; Non-AMB: Non-ambulant; NR: Not recorded; PFNA: Proximal femoral nail anti-rotation; ST: Subtrochanteric

*Underwent general anaesthesia.

†Male patient.

‡Bedbound or wheelchair bound.

In terms of comorbidities, hypertension, anaemia and osteoporosis were most common; 83.3% (n = 5) of Group A patients and 85.7% (n = 6) of Group B patients were anaemic. The CCI for Group A was 1.00 (range, 0 to 2) and 1.29 for Group B (range, 0 to 3), and were not significantly different (*P* value = 0.590). Mean CCI for the entire study group was 1.15.

Functionally, all patients in Group A (n = 6) were pre-morbidly ambulant and 1 patient could ambulate without walking aid. In Group B, 57.1% (n = 4) of the patients were pre-morbidly ambulant, 2 could ambulate without walking aid while the remainder 42.9% (n = 3) were non-ambulant, bed or chairbound.

Operative management was not pursued in Group B as 4 patients were pre-morbidly bed or wheelchair bound, 1 patient had a recent non-ST elevation myocardial infarction and 2 others had opted out of operative management.

Management Outcomes and Complications

With regards to mortality, 53.8% (n = 7) of the entire study group died from non-surgical-related complications. Mortality rates within 1 year from injury were consistently lower in Group A as shown in Table 3. Reasons for death in Group A include pneumonia and stroke, with earliest death at 97 days. Comparatively, 57.1% (n = 4) of Group B patients died from complications including ischaemic heart disease and pneumonia in 1 year. The earliest death in Group B occurred during admission at 9 days in a patient with femoral neck fracture (CCI = 1), cause of death being urinary tract infection complicated by septicaemia. Mean hospital stay of the study group patients was 14.2 days (range, 8 to 24 days) in Group A and 10.3 days (range, 5 to 22 days) in Group B.

Discussion

The CCI scores of centenarians in our study group tended to be low. This was also reflected in a previous study of 134,527 centenarian admissions within a 5-year period – 57% of admissions had mild comorbidity (CCI = 0 to 1), 39.3% had moderate comorbidity (CCI = 2 to 4) and 3.7% severe comorbidity (CCI ≥5).[5] Tarity et al also cited mean CCI score of 1.61 (range, 0 to 5) in a group of 23 centenarian patients sustaining hip fractures.[6] We postulate that centenarians tend to be healthier than most elderly patients and have lower CCI scores, since most of those with multiple comorbidities would have died earlier from complications of those diseases.

Table 3. Mortality and Survival of Patients

Time Period	Operative Group A (n = 6)	Conservative Group B (n = 7)	*P* Value*
Mortality			
Within 30 days	0%	14.3%	0.377
Within 90 days	0%	28.6%	0.182
Within 6 months	16.7%	42.8%	0.349
Within 1 year	33.3%	57.1%	0.433
Surviving patients			
Duration of survival post-injury (days)	97, 205, 1079	9, 62, 157, 237	0.939
Length of stay (days)	14.2	10.6	0.327

*P values of <0.05 is considered as statistically significant.

We found that mortality outcomes with operative management in Group A were lower than Group B within a 1-year interval from injury, which were consistent with findings in previous studies.[6,7] This was contrary to the common belief that centenarians generally have higher surgical risks due to their advanced age and are at higher risks of postoperative-related complications and mortality. Granted, the mortality rate was not statistically significant between both groups due to the small sample size.

Operative management resulted in 83% (n = 5) of Group A patients being able to achieve ambulation, as opposed to only 1 out of 4 Group B patients who were previously ambulant with or without walking aid. Since prolonged bed rest may increase immobility-related complications, surgery followed by early mobilisation remains the best option for these patients.[8,9]

One of the limitations of our study includes small sample size as the centenarian population are small in numbers. Secondly, CCI scores in this study were in the low range from 0 to 3 points and may not be applicable in patients with high CCI scores. With more centenarians in the future, further studies with comparison of larger groups of centenarians, nonagenarians (aged 90 to 99) and octogenarians (aged 80 to 89) will be useful to aid clinical decision-making.

Conclusion

Our study shows that the centenarian hip fracture population does not necessarily correlate with high surgical risk patients. In fact, operatively treated patients experienced consistently lower mortality rate within 1 year and also managed to better retain ambulatory ability. We advocate due consideration for surgical management of this patient group despite their advanced age in patients with few comorbidities.

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Adult Onset Sporadic Cerebellar Ataxia in Singapore: Diagnostic Outcomes of Paraneoplastic Antibody Testing and Early Clinical Features of Paraneoplastic Cerebellar Degeneration

Dear Editor,

The initial presentation of cerebellar ataxia remains a diagnostic challenge due to its multiple etiologies, one of which is paraneoplastic cerebellar degeneration (PCD), a rare neurological disease. Although paraneoplastic antibody testing may be helpful, seronegative PCD may account for up to 50% of PCD cases.[1]

The causes of ataxia in the Asian population differ from that of the Western population – the proportion of multiple system atrophy of the cerebellar type (MSA-C) relative to MSA with predominant parkinsonism (MSA-P) is higher[2] and Friedrich's ataxia is rare.[3] MSA-C can be difficult to diagnose at onset. In patients whose etiology cannot be determined, a diagnostic label of either idiopathic adult onset cerebellar ataxia (AOCA) or idiopathic late onset cerebellar ataxia (ILOCA) is usually applied. However, it is not uncommon for the etiology to remain unknown despite extensive investigations.[4]

This study aimed to determine the diagnostic outcomes in adult patients presenting with a subacute or chronic cerebellar ataxia for which the diagnosis was not readily apparent, thus, requiring paraneoplastic antibodies to be performed. We also investigated clinical features at onset that would allow us to distinguish PCD from sporadic degenerative ataxias.

Materials and Methods

A retrospective case note analysis was performed on patients referred to the National Neuroscience Institute between 1 January 2007 and 1 October 2014 who presented with a subacute or chronic progressive ataxia and had anti-neuronal antibodies performed as part of the diagnostic workup. Inclusion criteria included disease onset after the age of 20 years, absence of established symptomatic causes such as ischaemia, haemorrhage or tumour in the posterior fossa, alcohol abuse and chronic anticonvulsant use. Patients were excluded if there were other dominant neurological signs. Paraneoplastic antibodies that were tested included: Hu, Yo, Ri, CV2, amphiphysin, Ma2, Tr (EUROIMMUN and EUROLINE kits, EUROIMMUN AG, Luebeck, Germany). A subset of patients was also tested for voltage-gated calcium channel (VGCC) antibody and voltage-gated potassium (VGKC) antibody. The metabotropic glutamate receptor 1 (mGluR1) antibody was not tested.

Diagnoses of MSA-C, SAOA or ILOCA and PCD were made based on established clinical criteria.[4-6]

Ethical approval was obtained from the SingHealth Centralised Institutional Review Board.

Results

A total of 81 patients (48 male and 33 female) presented with a cerebellar syndrome which required further diagnostic workup. The anti-Yo antibody was positive in 3 (3.7%) patients. Four (4.9%) patients were diagnosed with PCD. The diagnostic outcomes are shown in Table 1.

The 4 patients diagnosed with PCD were between the ages of 60 and 75 with a mean age of 66 years and were

Table 1. Diagnostic Outcomes of Patients Presented with Subacute or Chronic Progressive Ataxia with Paraneoplastic Antibodies Testing Performed

Diagnosis	Number of Patients (n = 81)
MSA-C	20 (24.7%)
AOCA or ILOCA	9 (11.1%)
Infectious causes	6 (7.4%)
Paraneoplastic cerebellar degeneration	4 (4.9%)
Spinocerebellar ataxia	3 (3.7%)
SREAT	3 (3.7%)
Drug-related diagnoses	2 (2.5%)
Other diagnoses: cervical myelopathy, CADASIL, corticobasal degeneration, dementia, hypertrophic olivary degeneration, Issac's syndrome, limbic encephalitis, lumbar spondylosis, Parkinson's disease, progressive supranuclear palsy, sensory ataxia, Sjogren's syndrome and vestibulopathy	20 (24.7%)
Unexplained diagnoses	14 (17.4%)

AOCA: Adult onset cerebellar ataxia; CADASIL: Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy; ILOCA: Idiopathic late onset cerebellar ataxia; MSA-C: Multiple system atrophy of the cerebellar type; SREAT: Steroid-responsive encephalopathy associated with autoimmune thyroiditis

followed up for a mean of 2.67 years. Ovarian cancer was detected in 3 female patients who were anti-Yo antibody-positive patients while small cell cancer of the lung was detected in 1 male patient who was antibody negative. In all cases, malignancy was detected on the same clinical encounter with normal brain imaging at onset. All received intravenous immunoglobulin and chemotherapy with 1 patient also receiving intravenous methylprednisolone. Treatment response was poor; the patients required the use of a walking aid and wheelchair after a mean of 7 and 29 months, respectively. The last known functional status of these 4 patients was 1 was wheelchair bound, 1 required a walking aid, 1 was independent and 1 whose status was unknown. At the end of the follow-up period, only 1 patient (25%) remained alive.

A total of 29 patients, between the ages of 33 and 81, with a mean age of 63 years, were diagnosed with sporadic degenerative ataxias (MSA-C, AOCA and ILOCA); 14 (51.7%) were female. Brain imaging findings at onset include 16 (55.2%) with cerebellar atrophy, 8 (27.6%) were normal and 5 (17.2%) with non-specific changes. None had the hot cross bun sign seen initially. These patients required the use of a walking aid and wheelchair after a mean of 34.8 and 36 months, respectively. Six (20.7%) were wheelchair bound, 8 (27.6%) required a walking aid and 15 (51.7%) remained independent on the last follow-up. Twenty-six (89.7%) patients with sporadic degenerative ataxias remained alive at the end of the follow-up period.

Clinical features at onset in patients with PCD are compared with those with sporadic degenerative ataxias in Table 2. Statistical analyses were not performed due to small patient numbers.

Table 2. Comparison of the Prevalence of Clinical Features Seen at the Onset of PCD and Sporadic Degenerative Ataxias

	Paraneoplastic Cerebellar Degeneration (n = 4)	**Sporadic Degenerative Ataxias (n = 29)**
Cerebellar features		
Nystagmus	0 (0%)	8 (27.6%)
Dysarthria	1 (25%)	13 (44.8%)
Intention tremor	2 (50%)	19 (65.5%)
Gait ataxia	1 (25%)	22 (75.9%)
Truncal ataxia	3 (75%)	1 (3.4%)
Positive Romberg's	0 (0%)	4 (13.8%)
Extrapyramidal features		
Parkinsonism	0 (0%)	10 (34.5%)
Dystonia	0 (0%)	0 (0%)
Autonomic features		
Autonomic dysfunction	0 (0%)	8 (27.6%)
Urinary incontinence	0 (0%)	2 (6.9%)
Orthostatic hypotension	0 (0%)	6 (20.7%)
Erectile dysfunction	0 (0%)	1(3.4%)
Other features		
Cognitive impairment	0 (0%)	2 (6.9%)
Cranial nerve involvement	0 (0%)	1 (3.4%)
Motor symptoms	0 (0%)	3 (10.3%)
Sensory symptoms	1 (25%)	1 (3.4%)

PCD: Paraneoplastic cerebellar degeneration

Discussion

In patients presenting with a cerebellar syndrome for which the initial diagnosis was unclear and paraneoplastic antibody testing was performed, 4 cases of PCD were detected, of which 3 were positive for the anti-Yo antibody. We detected only 1 case of seronegative PCD. In all 4 cases, the primary tumour was detected in the same clinical encounter. This was in contrast to previous studies where the majority of PCD cases either occurred before the eventual diagnosis of cancer, or occurred in patients with a known history of cancer.[7,8] In this study, the number of PCD cases was underestimated as patients with known malignancies under regular surveillance by the oncologists tend not to have further confirmation of PCD with antibody testing.

There has not been any previously published study investigating the yield of antibody testing in patients presenting with a cerebellar syndrome. Our pick-up rate of 3.7% is high for this rare disease. Previous studies screening for a broad range of paraneoplastic disorders had a much lower pick-up rate – in a study by Shams'ili et al, more than 5000 samples were screened, of which 137 patients were antibody positive.[8] However, the population screened was heterogeneous with a range of clinical presentations.

The most common diagnostic outcome was MSA-C (24.7%). Our findings are consistent with other studies performed in the Western population where MSA-C remains a common diagnosis in patients initially thought to have sporadic adult onset ataxia.[9] The high proportion of patients with unexplained ataxia in our study is consistent with a previous study.[9] Although extensive genetic testing was not performed in our local context, it is unlikely that this would alter the proportion of cases with unexplained ataxia as further genetic testing in this population is low yield.[10]

Early clinical features that favoured a diagnosis of PCD over sporadic degenerative ataxias included the female gender, rapidly progressive symptoms, normal brain imaging at onset, truncal ataxia, absence of nystagmus, dysarthria, parkinsonism and autonomic features, which are

consistent with previous studies.[8] Normal brain imaging in the presence of clinically severe disease has been found to be predictive of PCD[11,12] while cases in which brain imaging was abnormal at onset are rare.[13,14] It has been recommended that the diagnosis of PCD must be suspected in all patients with subacute and rapid progression of ataxia.[8] Although disease progression is most rapid in MSA-C amongst other causes of sporadic degenerative ataxias,[15] PCD has a more rapid progression compared to MSA-C.

The limitation of this study was the small patient numbers. This was a real-world study examining the clinical outcomes in patients presenting with subacute or chronic ataxia who had paraneoplastic antibodies tested. However, this could be influenced by individual and institutional practices. Prospective studies examining patients at onset would be helpful. The relatively high pick-up rate of antibody testing underscores the utility of testing such patients for PCD.

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