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"In solitude, the mind gains strength and learns to lean upon itself."

Laurence Sterne (1713 - 68)
Irish novelist

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Editorial

Depression: Let's Talk

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On April 7 each year, the World Health Organization commemorates its founding with World Health Day and the theme for this year is depression. As described at its website: "Depression affects people of all ages, from all walks of life, in all countries. It causes mental anguish and impacts on people's ability to carry out even the simplest everyday tasks, with sometimes devastating consequences for relationships with family and friends and the ability to earn a living. At worst, depression can lead to suicide, now the second leading cause of death among 15 to 29 year olds".

According to the 2010 Singapore Mental Health Study (SMHS), a nationally representative survey of adult Singapore residents aged 18 years and above, depression is indeed common in our local population. Using the World Mental Health Composite International Diagnostic Interview (a structured diagnostic instrument), the prevalence of major depressive disorder (MDD) in the general population was 5.8%. It was significantly higher among females, Indians, those who were divorced/separated, or widowed. Chronic physical conditions were present in approximately half of those with MDD.[1]

Other than the individual personal costs, the societal impact of depression stems from its relative pervasiveness among the population; from its early onset (typically starting in adolescence or early adult life), recurrent nature and its multifarious impairments—often leading to substantial loss in quality of life and premature death.[2]

In the SMHS, we found that MDD was also associated with considerable disability in terms of days of role impairment and considerable economic losses that come from the loss of productivity. Depression represents one of the major causes of loss of productivity in the workplace from both absenteeism (loss of production caused by days missed from work) and presenteeism (loss of production caused by reduced work performance while at work as a result of decreased concentration, reduced motivation, fatigue, or errors in decision-making)—all of which constitutes a substantial cost to employers.[3]

One of the startling findings of the SMHS was that about 60% of those with MDD had never sought any form of professional help. There are various reasons for this treatment gap.

One of the important determinants of help-seeking is how a person perceives the nature and cause of symptoms which in turn may be influenced by the prevailing culture. It has been suggested that Asians tend to focus on physical (somatic) features of depression (like fatigue, loss of appetite and weight) than on the emotional or psychological symptoms—which understandably would not lead them to seek help from professional mental health providers.[4] In a subsequent study that assessed the level of mental health literacy among the general population of Singapore, we found that the common perception about a person suffering from depression as expressed by the majority of the members of the public was that the person is "weak" rather than sick.[5] The corollary is that someone with depression could get better on their own will, and if not, the person is lacking in fortitude and resilience.

So, people with depression would feel ashamed and to circumvent the stigma associated with depression, there is 'label avoidance' (i.e. people are reluctant to be diagnosed with or be seen as seeking treatment for depression). Stigma has been linked to adverse outcomes for people with mental illness as it acts as a barrier to help-seeking.[6]

Addressing and overcoming these barriers to appropriate help-seeking is obviously important, particularly when there are effective treatments including proven antidepressant medications and psychotherapies.

On the issue of treatment, there is perhaps, in our opinion (and in absence of any good studies), a predilection among local psychiatrists for the use of medications over psychotherapy. Antidepressant drugs are generally effective only as long as the treatment is continued. On the other hand, psychotherapy, especially cognitive behavioural therapy (CBT) provides long-term benefits probably because patients learn and internalise skills that they continue using after the treatment stops. Consequently, discontinued CBT might be as effective as continued treatment with antidepressant medication and more effective than antidepressant medication that is discontinued.[7] However,

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the question which is yet to be answered pertains to the extent that high quality CBT is used for depressed patients in Singapore—something that needs to be addressed with research that would assess not just the availability of CBT but its effectiveness (including cost-effectiveness) for our local patients. Another possible limitation is the acceptability of CBT by some patients who want and expect a "quick fix" for their depression, and/or are unable to commit the amount of time for CBT.

Still, there are limitations to the current treatment: it has been estimated that, even under optimal conditions, contemporary treatments can reduce only about one-third of the disease burden associated with MDD.[8,9] A way to further reduce the disease burden of depression would be to reduce the incidence through prevention. There are different types of prevention: universal prevention which focuses on the general population and selective prevention that targets individuals or subgroups that are at higher risk of developing mental disorders than average individuals or subgroups. A meta-analysis of 32 randomised controlled trials examining the effects of preventive, psychological interventions in participants with no diagnosed depression at baseline (but deemed to be "at risk" of becoming depressed, as assessed with a diagnostic instrument) on the incidence of diagnosed depressive disorders at follow-up found that these preventive interventions lowered the incidence of depression by 21% in the intervention group compared with controls.[10]

Moving forward, what would be important from the perspective of population health, is to narrow the treatment gap for depression which calls for a raft of initiatives that specifically target those groups in the populations where depression is over represented. It also calls for an effort to combat stigma with a concerted and collaborative political, social, medical and media will and efforts. Early detection/screening systems should be established in schools, polyclinics, general hospitals and workplaces. It is important for businesses to understand the economic case for the detection and treatment of depression among their employees and be cognisant of the existing literature supporting the economic case for employers to invest in interventions to address depression in the workplace.[11] However, most employers would not know how to do this and would need expert help such as that rendered by The Partnership for Workplace Mental Health, an initiative by the American Psychiatric Association that helps employers in raising awareness and reducing stigma.

Other innovative ways to improve the rates for treatment contact ought to be considered. This includes the use of Internet and telephone-delivered therapy which have the advantage of alleviating the fear of loss of privacy and lack of confidentiality (although, of course, more research is needed to evaluate the efficacy and effectiveness of such non face-to-face therapy in the local population).

More research is also needed (especially qualitative research) to elucidate the social, cultural, and religious factors that might influence help-seeking behaviour and the stigma of depression; as well as studies to test out preventive strategies that are contextualised to the local setting.

Depression is a condition that has long been recognised to be a public health problem worldwide which is expected to worsen in the future. Between 1990 and 2010, major depression moved up from 15th to 11th in terms of global disease burden measured in disability-adjusted life years (DALYs).[12] By 2030, it is projected to become the single leading cause of disease burden.[13]

However, with our existing knowledge and with a concerted and determined effort to understand more and to do more (through enlightened mental health policies, funded programme development and evaluation and research), we might be able to bend the curve for our own population.

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Original Article

Comparison of the Minimally Invasive and Conventional Open Surgery Approach in the Treatment of Lumbar Stenosis: A Systematic Review and a Meta-Analysis

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Abstract

Introduction: Minimally invasive surgery (MIS) is increasingly used in the treatment of lumbar stenosis. However, it is still not clear if the employment of minimally invasive surgical techniques can achieve superior clinical outcomes compared to standard open laminectomy. Materials and Methods: An extensive literature review regarding the clinical outcome, safety, and efficiency of MIS and standard open surgery (OS) in the treatment of lumbar stenosis was conducted on Medline, Cochrane, EMBASE, and Google Scholar databases up to 19 August 2016. Results: Sixteen studies that enrolled a total of 1580 patients with surgically-indicated lumbar stenosis were identified; 793 patients underwent MIS and 787 patients underwent conventional OS. No significant difference was found in the improvement of Oswestry Disability Index (ODI) ($P = 0.718$) and operation time ($P = 0.322$) between patients from different treatment groups. MIS was associated with better visual analogue scale (VAS) for back pain ($P = 0.01$), shorter length of hospital stay ($P < 0.001$), and lower blood loss ($P < 0.001$). Conclusion: Our findings indicate that both MIS and standard OS can effectively manage patients with lumbar stenosis and lead to comparable clinical outcomes. Further studies are necessary to evaluate MIS with different types of conventional surgery for lumbar stenosis.

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Key words: Back pain, Laminectomy

Introduction

Spinal stenosis is a narrowing of the spinal canal with encroachment on the neural structures by surrounding osseous, discal, capsular, or ligamentous structures. Clinical symptoms include radicular leg pain and neurogenic claudication. The prevalence of this condition is growing as the population continues to age. Indications for surgery vary widely across geographic areas.[1] Although significant controversy exists regarding the management of lumbar spinal stenosis, it is still the most common reason for lumbar spine surgery in adults over the age of 65 years.[2,3] However, the optimal surgical procedure for the treatment of lumbar spinal stenosis is still to be determined. The current standard approach are open laminectomy, medial facetectomy, and foraminotomy, with extensive removal of posterior spinal structures.[4] The obvious advantage of the open approach is an excellent visualisation and access to damaged tissues; however, a substantial rate of postoperative complications has been reported to be associated with this procedure.[5,6] Also, extensive disruption of spine and supporting muscle structures may lead to adverse consequences, such as flexion instability, muscle weakness, and failed back surgery syndrome.[7-9]

As an alternative to standard open surgery (OS), endoscopic and minimally invasive surgical techniques have been developed. Minimally invasive surgery (MIS) procedures use muscle-splitting to access the spine, and leave the midline structures that support muscles and ligaments intact, resulting in less tissue trauma, reduced blood loss, faster recovery times and shorter hospital stays compared to standard OS.[10] In addition, the possibility that the patient can be discharged on the same day as surgery can significantly reduce healthcare costs. Potential issues with MIS is that mastering the techniques requires additional training times,[7,11] and it is not clear if employment of MIS techniques can lead to superior clinical outcomes compared

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to OS. The objective of our study was to compare standard open laminectomy with the MIS approach in regard to clinical outcome, safety, and efficiency.

Materials and Methods

Search Strategy

We followed the PRISMA guidance for systematic reviews of observational and diagnostic studies,[12] and searched the published literature using Medline, Cochrane, EMBASE, and Google Scholar up to 19 August 2016, with various combinations of the following key words: lumbar stenosis, minimally invasive surgery (MIS), conventional OS, laminectomy, fusion. In addition, we manually searched references in relevant publications to identify additional eligible trials. Inclusion criteria for the meta-analysis were randomised controlled trials (RCTs), prospective studies, and cohort studies that recruited patients with surgically-indicated lumbar stenosis who underwent surgical decompression with minimally invasive or conventional OS. Letters, comments, editorials, case reports, proceedings, personal communications, as well as studies that did not provide quantitative outcome were excluded.

Study Selection and Data Extraction

Data was extracted independently by 2 independent reviewers. A third reviewer was consulted in cases of disagreements. We extracted data on study population (number, age, and gender of subjects in each group), study design, and the major outcomes.

Quality Assessment

We assessed the RCT study quality using the Cochrane Risk of Bias Tool,[13] and used Newcastle-Ottawa scale[14] to assess the quality of non-RCTs. The quality assessment was performed by 2 independent reviewers, and a third reviewer to decide any disagreements.

Outcome Measures

The primary outcomes included the level of improvement of Oswestry Disability Index (ODI) and visual analogue scale (VAS) for back and leg pain. Secondary outcomes included operation time, length of hospital stay, blood loss, and complications.

Statistical Analysis

Peto odds ratios (POR) with 95% confidence intervals (CI) were calculated for dichotomous outcome variables (complications) between patients who underwent either minimally invasive or conventional surgery. For continuous outcomes, the differences in means with 95% CI between the 2 groups were calculated for each individual study and for all studies combined.

Heterogeneity Assessment

We performed a χ^2-based homogeneity test and determined the Q statistics and the inconsistency index (I^2). A random-effects model was used when the I^2 statistic was >50%. The fixed-effect model was employed otherwise. Pooled effects were calculated and a two-sided P value <0.05 was used to indicate statistical significance. Sensitivity analysis was carried out using the leave one-out approach. Publication bias was assessed for the primary outcomes by constructing funnel plots by Egger's test. The absence of publication bias was indicated by the data points forming a symmetric funnel-shaped distribution and one-tailed significance level P >0.05 (Egger's test). However, the publication bias analysis was not performed for the secondary outcomes due to the limited number of studies.[15] In addition, subgroup analysis was performed per the type of conventional OS (transforaminal lumbar interbody fusion [TLIF] or laminectomy [decompression]). All analyses were performed using Comprehensive Meta-Analysis statistical software, version 2.0 (Biostat, Englewood, NJ, USA).

Results

Of the 815 articles initially identified, 765 were excluded for not being relevant after initial review of abstracts and titles (Fig. 1). Fifty studies were fully reviewed and 34

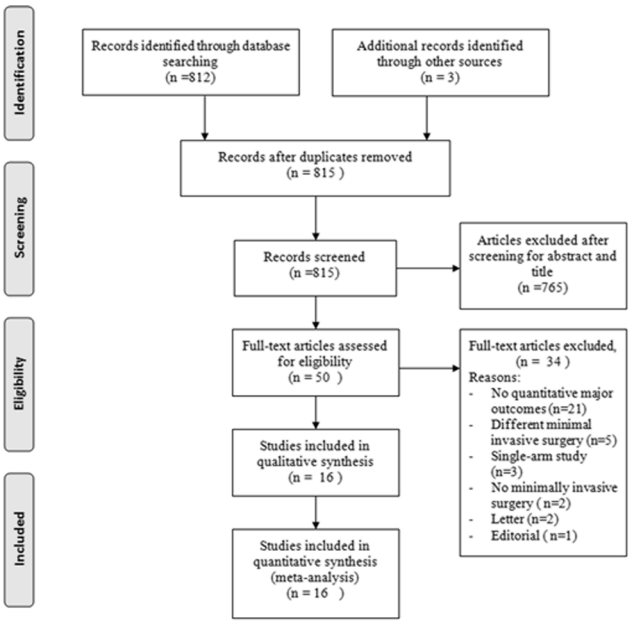

Fig. 1. PRISMA flow diagram.

Table 1. Summary of Basic Characteristics of Studies Selected for Meta-Analysis

First Author (Year)	Study Design	Comparison Group	Surgical Technique	No. of Patients	Age (Year)	Male (%)	Symptom Duration (Month)	Operated Level	Length of Follow-up (Month)	Newcastle-Ottawa Scale
Ang (2015)	NRCT	MIS	Minimally invasive lumbar laminotomy	83	58.1*	35%	NA		NA	8
		Conventional OS	Open lumbar laminotomy	30	54.7*	33%	NA	Single level	24	
Kim (2015)	NRCT	MIS	Microsurgical extraforaminal decompression	25	73	36%	13.67	L3 – L4:3; L4 – L5:13; L5 – S1:9	NA	9
		Conventional OS	Posterior lumbar interbody fusion	30	70	30%	14.42	L1 – L2:1; L3 – L4:1; L4 – L5:14; L5 – S1:14	NA	
Luo (2015)	RCT	MIS	MIS-TLIF using a tubular retraction system	42	64.4	55%	NA		26	NA
		Conventional OS	TLIF	54	66.5	59%	NA		27	
Nerland (2015)	NRCT	MIS	Microdecompression	246	68	58%	NA	L2/3: 13; L3/4: 126; L4/5: 203; L5/S1: 20	1y	9
		Conventional OS	Laminectomy	246	69	53%	NA	L2/3: 18; L3/4: 116; L4/5: 197; L5/S1: 26		
Hu (2014)	NRCT	MIS	Percutaneous intervertebral foramina endoscopic lumbar discectomy decompression	30	65	57%	5.3	L3/4: 12; L4/5: 15; L5/S1: 20	NA	9
		Conventional OS	Traditional surgery	30	67	50%	5.9	L3/4: 14; L4/5: 17; L5/S1: 21	NA	
Mobbs (2014)	RCT	MIS	Minimally invasive unilateral laminectomy for bilateral decompression	27	73	22%	NA	L2/3: 1; L3/4: 5; L4/5: 23; L5/S1: 0	36.9	NA
		Conventional OS	Conventional laminectomy	27	66	14%	NA	L2/3: 4; L3/4: 8; L4/5: 21; L5/S1: 3	44.3	
Singh (2014)	NRCT	MIS	MIS-TLIF	33	51.7	70%	NA	Single level	NA	7
		Conventional OS	Open-TLIF	33	49.9	64%	NA		NA	

MIS: Minimally invasive surgery; NA: Not applicable; OS: Open surgery; RCT: Randomised clinical trial; TLIF: Transforaminal lumbar interbody fusion

*Value presented as median.

Table 1. Summary of Basic Characteristics of Studies Selected for Meta-Analysis (Cont'd)

First Author (Year)	Study Design	Comparison Group	Surgical Technique	No. of Patients	Age (Year)	Male (%)	Symptom Duration (Month)	Operated Level	Length of Follow-up (Month)	Newcastle-Ottawa Scale
Wen (2014)	NRCT	MIS	Unilateral decompression via fenestration under quadrant retractor	32	56	41%	NA	One level: 23; two level: 9	32.8	9
		Conventional OS	Open decompression with fusion and internal fixation	50	57.8	36%	NA	One level: 38; two level:12		
Archavlis (2013)	NRCT	MIS	MIS-TLIF	24	67	42%	NA	L3 – 4: 2; L4 – 5: 16; L5 – S1: 6	26	9
		Conventional OS	Open-TLIF	25	68	32%	NA	L3 – 4: 1; L4 – 5: 17; L5 – S1: 7	26	
Yang (2013)	NRCT	MIS	MIS-TLIF	43	55	35%	38		21	7
		Conventional OS	Open-TLIF	104	52	36%	40		23	
Ercegovic (2012)	NRCT	MIS	Minimally invasive decompression	51	55.7	47%	33.5	One level, 82.4%; Multiple levels, 17.6%	NA	7
		Conventional OS	Formal laminectomy	22	55.8	59%	28.4	One level, 45.5% ; Multiple levels, 54.5%	NA	
Harris (2011)	NRCT	MIS	Mini-open technique, with a small, central incision	30	66	33%	NA	Single level, L4/5	NA	9
		Conventional OS	Standard, midline open technique	21	69.1	43%	NA		NA	

MIS: Minimally invasive surgery; NA: Not applicable; OS: Open surgery; RCT: Randomised clinical trial; TLIF: Transforaminal lumbar interbody fusion

*Value presented as median.

Table 1. Summary of Basic Characteristics of Studies Selected for Meta-Analysis (Cont'd)

First Author (Year)	Study Design	Comparison Group	Surgical Technique	No. of Patients	Age (Year)	Male (%)	Symptom Duration (Month)	Operated Level	Length of Follow-up (Month)	Newcastle-Ottawa Scale
Wang (2011)	NRCT	MIS	Minimally invasive transforaminal lumbar fusion	25	55	52%	NA	L3 – L4: 2; L4 – L5: 11; L5 – S1: 9	27.5	9
		Conventional OS	Open transforaminal lumbar interbody fusion	27	56	56%		L3 – L4: 2; L4 – L5: 11; L5 – S1: 10		
Yang (2011)	Non-RCT	MIS	Microendoscopic decompression via unilateral	42	54	57%	11.7*	L2/3: 2; L3/4: 4; L4/5: 18; L5/S1: 16; L4-S1:2	16	9
		Conventional OS	Posterior lamina fenestration decompression	37	57	54%	14.2*	L2/3: 2; L3/4: 5; L4/5: 12; L5/S1:15; L3 – 5:1; L4 – S1: 2		
Yagi (2009)	RCT	MIS	Modified unilateral-approach midline decompression microendoscopic laminectomy	20	73	40%	NA		17.8	NA
		Conventional OS	Conventional open laminectomy	21	71	29%	NA		18.6	
Cho (2007)	RCT	MIS	Split-spinous process laminotomy and discectomy	40	61	40%	NA	2.45 ± 0.68	15.1	NA
		Conventional OS	Conventional open laminectomy	30	59	50%	NA	2.56 ± 0.50	14.8	

MIS: Minimally invasive surgery; NA: Not applicable; OS: Open surgery; RCT: Randomised clinical trial; TLIF: Transforaminal lumbar interbody fusion

*Value presented as median.

Table 2. Summary of Outcomes in Studies Selected for Meta-Analysis (MIS Versus Conventional OS)

	Improvement (MIS Vs Conventional OS)			Operation Time (Min)	Length of Hospital Stay (Day)	Estimated Intraoperative Blood Loss (mL)
	ODI	VAS-Back	VAS-Leg			
Ang (2015)	26 vs 28	1.5 vs 4.0	6.0 vs 5.0	65 vs 65	1.1 vs 3.0	NA
Kim (2015)	21 vs 26	1.7 vs 3.2	4.8 vs 4.1	NA	NA	NA
Luo (2015)	56 vs 54	5.2 vs 4.9	NA	96 vs 83	NA	175 vs 296
Nerland (2015)	19 vs 17	NA	NA	One: 6.9; Two: -14.2	One: 1.6; Two: 2.0	NA
Hu (2014)	26 vs 27	NA	NA	60 vs 90	4.3 vs 9.5	13 vs 201
Mobbs (2014)	29 vs 18	NA	5.6 vs 3.9	NA	100.8 hour vs 55.1 hour	NA
Singh (2014)	NA	4 vs 4.8	NA	115.8 vs 186		124 vs 380
Wen (2014)	40 vs 41	4.7 vs 4.6	5.2 vs 5.1	52 vs 153	8.2 vs 8.6	25 vs 345
Archavlis (2013)	23 vs 24	4.4 vs 3.8	4 vs 3.8	220 vs 190	NA	185 vs 255
Yang (2013)	44 vs 43	6.6 vs 6.3	NA	175 vs 177	96 vs 170	362 vs 720
Ercegovic (2012)	NA	4.5 vs 2.7	NA	NA	NA	NA
Harris (2011)	32 vs 39	NA	5.5 vs 5.2	150 vs 156	2.5 vs 3.2	208 vs 335
Wang (2011)	27 vs 26	5.8 vs 5.4	NA	139 vs 143	NA	291 vs 652
Yang (2011)	41 vs 42	3.4 vs 2.4	NA	50 vs 75	9.4 vs 12.1	80 vs 140
Yagi (2009)	NA	NA	NA	71 vs 64	3.9 vs 12.5	37 vs 71
Cho (2007)	NA	4.1 vs 3.1	NA	259 vs 193	4 vs 7.2	154 vs 132

MIS: Minimally invasive surgery; NA: Not applicable; ODI: Oswestry Disability Index; OS: Open surgery; VAS: Visual analogue scale

were excluded for being a letter, being a single-arm study, reporting outcomes other than MIS, or not presenting outcomes quantitatively. Sixteen studies were included in the analysis.[16-31]

Study Characteristics

The 16 studies included 4 RCTs[17,22,23,25] and the remaining were non-RCTs.[18,20-24,27] All together, the studies included 1580 patients who had surgically-indicated lumbar stenosis. Of these, 793 patients underwent a MIS and 787 had conventional OS (n = 523 for laminectomy and n = 264 for TLIF). The basic characteristics of the studies are summarised in Table 1. The mean age ranged from 50 to 73 years and the percentages of male patients ranged from 14% to 70%. A summary of primary and secondary outcomes of selected studies are presented in Table 2.

Meta-Analysis

Oswestry Disability Index (ODI)

For ODI, 5 studies, (Singh [2014], Ercegovic [2012], Harris [2011], Yagi [2009] and Cho [2007]), were excluded due to lack of mean and standard deviation data. There was no evidence of heterogeneity across studies with regard to ODI (Q = 9.301, I^2 = 0%), therefore, a fixed-effect model of analysis was used. The overall analysis revealed no significant difference in the improvement of ODI between patients in the MIS and conventional OS groups (pooled difference in means = -0.18, 95% CI = -1.13 to 0.78, P = 0.718) (Fig. 2A). Four studies presented data for patients who received TLIF. Subgroup analysis comparing MIS and TLIF found no significant difference in ODI between the 2 groups (pooled difference in means = 0.50, 95% CI = -0.87 to 1.88, P = 0.473). Seven studies reported findings with respect to decompression surgery. Pooled analysis found ODI improvement was similar between patients who had MIS and those who had conventional decompression surgery (pooled difference in means = -0.81, 95% CI = -2.13 to 0.52, P = 0.233).

Visual Acuity Score

Significant heterogeneity in VAS for back and leg pain among the studies was observed (heterogeneity test: I^2 = 85.77% and 57.19% for back pain and leg pain, respectively); therefore, random effects models were used. The overall analysis revealed patients treated with MIS had significant better improvement of back pain than those who underwent conventional OS (pooled difference in means = 0.32, 95% CI = 0.08 to 0.56, P = 0.010) (Fig. 2B). Pooled data from studies that reported TLIF results (n = 3) found MIS showed greater improvement in back pain than conventional surgery (pooled difference in means = 0.34, 95% CI = 0.09 to

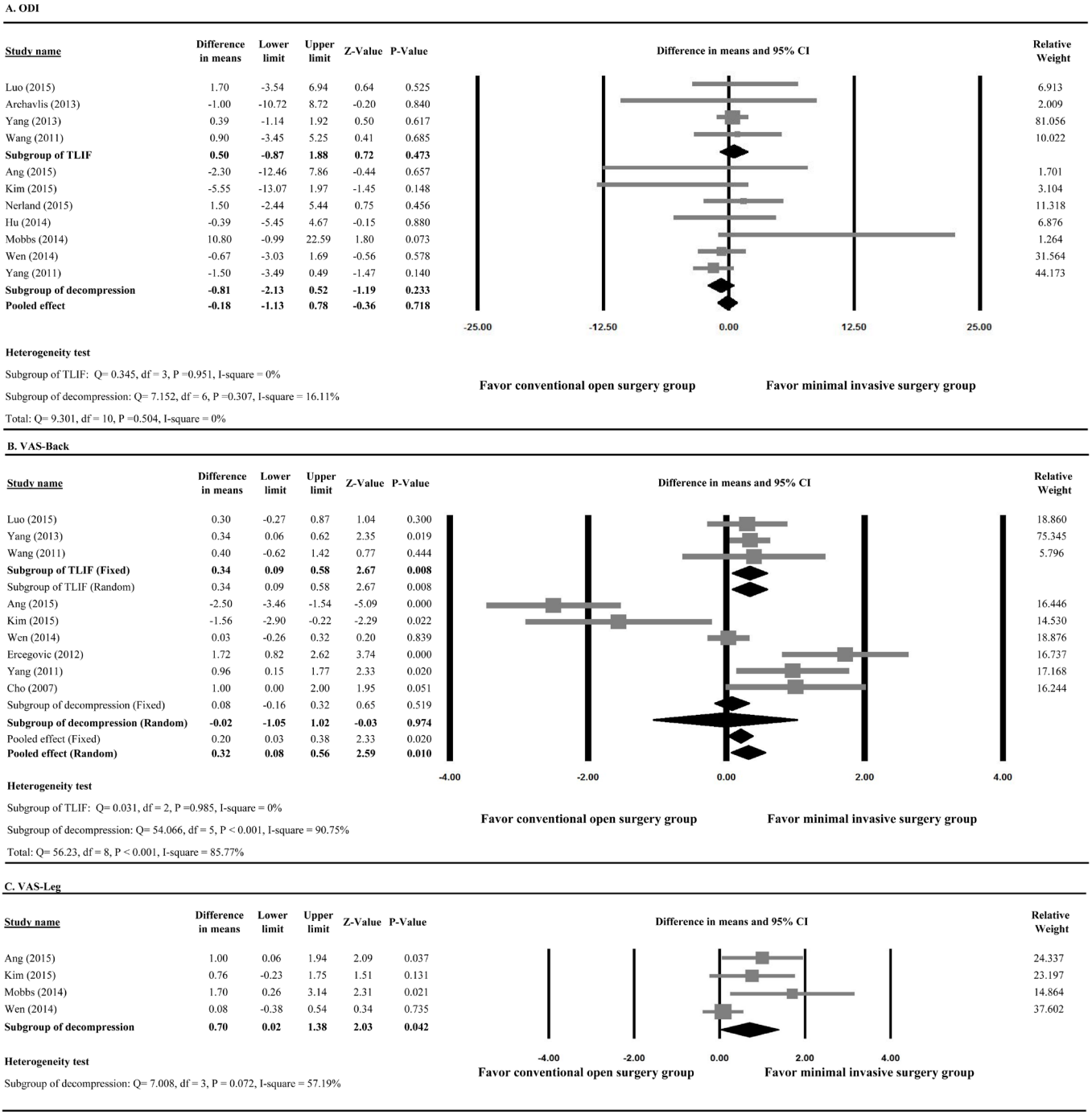

Fig. 2. Meta-analysis for primary outcomes. A) ODI; B) VAS-Back; C) VAS-Leg.

0.58, $P = 0.008$). In contrast, pooled analysis of data from the 6 studies that presented VAS for back pain following conventional decompression surgery found VAS results were similar between the 2 groups (pooled difference in means = -0.02, 95% CI = -1.05 to 1.02, $P = 0.974$).

Four studies reported VAS for leg pain. The studies evaluated MIS and conventional decompression surgery. Pooled analysis indicated patients treated with MIS had significant improvement in leg pain than those who underwent conventional decompression surgery (pooled difference in means = 0.70, 95% CI = 0.02 to 1.38, $P = 0.042$) (Fig. 2C).

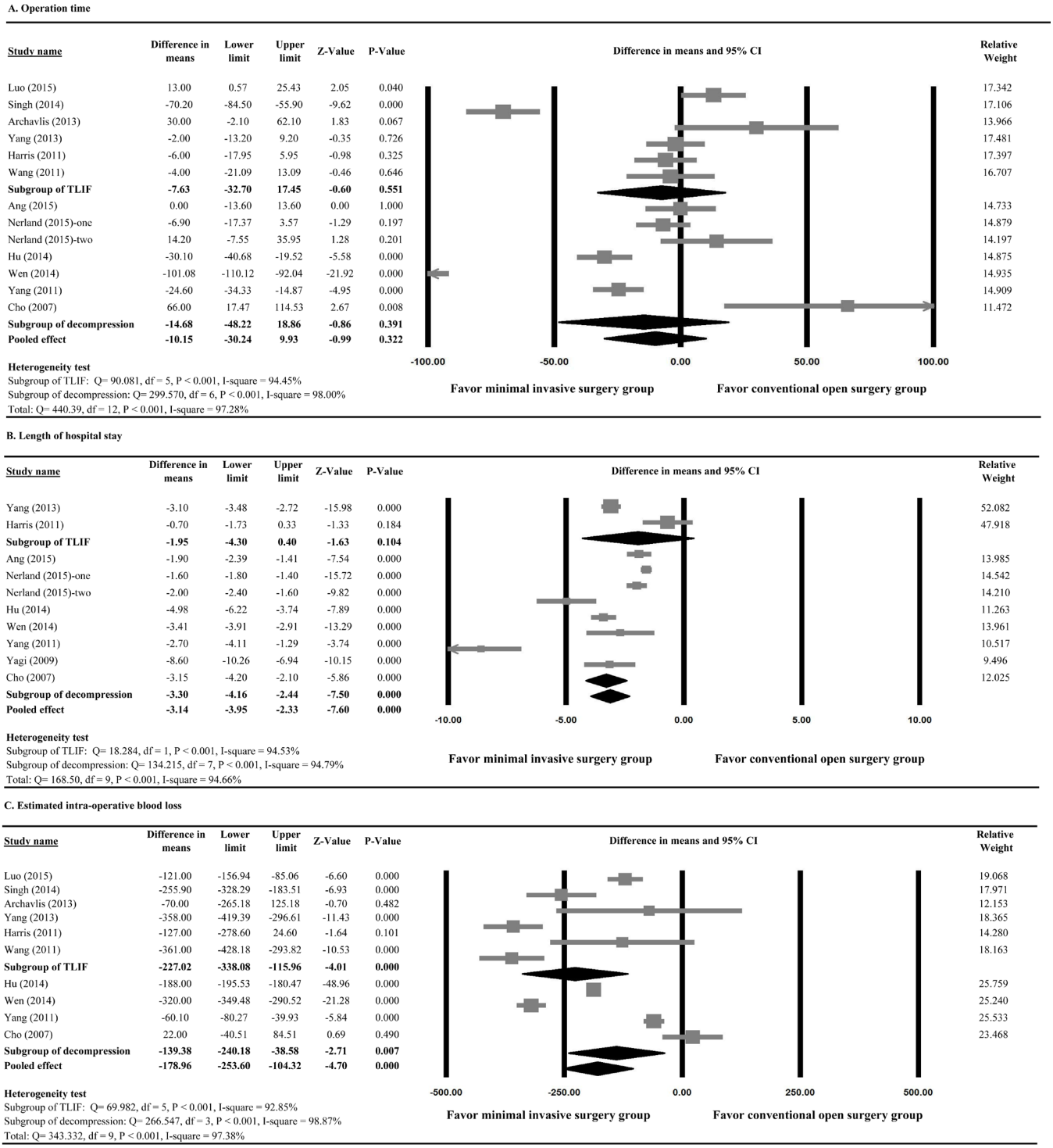

Fig. 3. Meta-analysis for secondary outcomes. A) Operation time; B) Length of hospital stay; C) Estimated intraoperative blood loss.

Meta-Analysis for Secondary Outcomes

Random effects models were used for analysis of operation time, length of hospital stay, and intraoperative blood loss due to high heterogeneity among the studies (heterogeneity tests: I^2 = 97.28%, 94.66% and 97.38% for operation time, length of hospital stay and intraoperative blood loss, respectively). The overall analysis revealed that patients who received MIS had shorter operation time than those who underwent conventional OS; however, the findings did not reach statistical significance (pooled difference in mean = -10.15, 95% CI = -3.24 to 9.93, P = 0.322) (Fig. 3A). Patients treated with MIS had shorter lengths

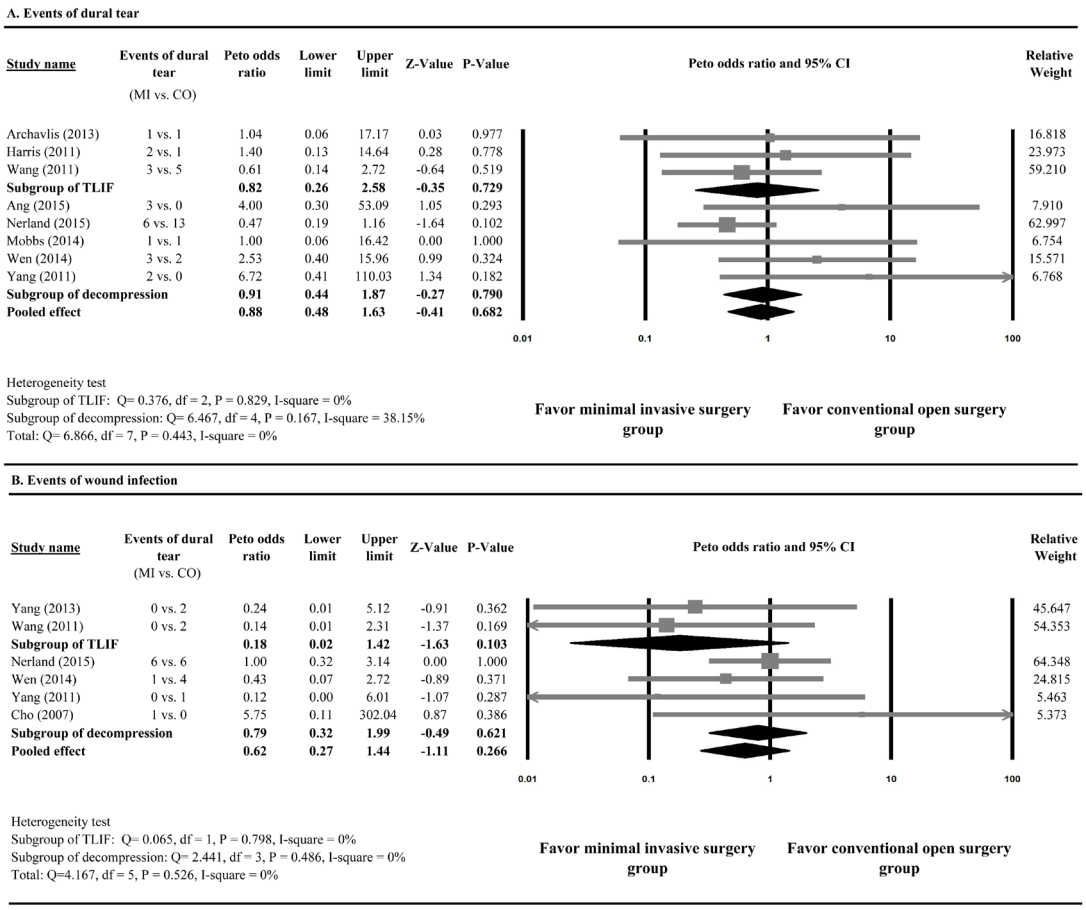

Fig. 4. Meta-analysis for safety outcomes. A) Dural tear; B) Wound infection.

of hospital stay (pooled difference in mean = -3.14, 95% CI = -3.95 to -2.33, P <0.001) (Fig. 3B) and lower blood loss than those who underwent conventional OS (pooled difference in mean = - 178.96, 95% CI = -253.60 to -104.32, P <0.001) (Fig. 3C).

For patients in the TLIF subgroup, no significant difference in the operation time and length of hospital stay were observed compared with MIS (P = 0.551 and P = 0.104, respectively). In contrast, patients treated with MIS had shorter lengths of hospital stay (pooled difference in mean = -3.30, 95% CI = -4.16 to -2.44, P <0.001) (Fig. 3B) and lower blood loss than those who underwent decompression surgery (pooled difference in mean = -139.38, 95% CI = -240.18 to -38.35, P = 0.007; Fig. 3C).

Meta-Analysis for Safety Outcomes

There was no significant heterogeneity in rates of dural tear and wound infection across studies (heterogeneity test: Q = 6.866, I^2 = 0% for dural tear and Q = 4.167, I^2 = 0% for wound infection); therefore, a fixed-effect model of analysis was used. Overall analysis revealed no significant differences in the rates of dural tear and wound infection between the MIS and conventional OS groups (Fig. 4). No significant differences in the rates of dural tear and wound infection between the TLIF or conventional decompression groups compared with MIS were observed.

Sensitivity Analysis

With the exception of VAS for leg pain, the direction and magnitude of combined estimates did not vary markedly with the removal of the individual studies, indicating that the meta-analysis was robust and the data were not overly influenced by each study. Removal of Ang et al (2015), Kim et al (2015) and Mobbs et al (2014) studies in turn influenced the findings for VAS leg pain (Table 3).

Quality Assessment

For the non-RCTs, the Newcastle-Ottawa scale score ranged from 7 to 9, out of 12 (Table 1) suggesting the studies were of good quality. Quality assessment of the RCTs indicated that 3 studies had random sequence generation and low risk for attrition and reporting bias (Fig. 5A). Half the

Table 3. Sensitivity Analysis

First Author (Year)	Statistics with Study Removed				
	Points	Lower Limit	Upper Limit	Z Value	*P* Value
ODI					
Ang (2015)	-0.16	-1.12	0.80	-0.32	0.748
Kim (2015)	-0.09	-1.05	0.87	-0.18	0.858
Luo (2015)	-0.24	-1.21	0.73	-0.49	0.627
Nerland (2015)	-0.28	-1.27	0.70	-0.56	0.576
Hu (2014)	-0.17	-1.14	0.80	-0.34	0.735
Mobbs (2014)	-0.25	-1.21	0.71	-0.51	0.611
Wen (2014)	-0.08	-1.12	0.97	-0.15	0.882
Archavlis (2013)	-0.17	-1.13	0.79	-0.34	0.731
Yang (2013)	-0.54	-1.76	0.68	-0.86	0.389
Wang (2011)	-0.23	-1.21	0.75	-0.46	0.644
Yang (2011)	0.22	-0.87	1.31	0.39	0.695
VAS-back					
Ang (2015)	0.43	0.03	0.84	2.10	0.036
Kim (2015)	0.28	-0.26	0.82	1.03	0.302
Luo (2015)	0.11	-0.51	0.73	0.35	0.725
Wen (2014)	0.14	-0.58	0.86	0.37	0.708
Yang (2013)	0.09	-0.64	0.82	0.24	0.808
Ercegovic (2012)	-0.03	-0.57	0.50	-0.12	0.903
Wang (2011)	0.11	-0.47	0.69	0.37	0.709
Yang (2011)	0.04	-0.54	0.62	0.13	0.898
Cho (2007)	0.05	-0.53	0.62	0.16	0.872
VAS-leg					
Ang (2015)	0.64	-0.22	1.50	1.47	0.143
Kim (2015)	0.75	-0.18	1.68	1.58	0.114
Mobbs (2014)	0.49	-0.12	1.10	1.56	0.118
Wen (2014)	1.03	0.42	1.65	3.29	0.001
Operation time					
Ang (2015)	-12.40	-36.00	11.20	-1.03	0.303
Luo (2015)	-13.62	-36.67	9.43	-1.16	0.247
Nerland (2015)-one	-11.72	-35.94	12.51	-0.95	0.343
Nerland (2015)-two	-13.60	-36.65	9.45	-1.16	0.248
Hu (2014)	-9.65	-34.23	14.93	-0.77	0.441
Singh (2014)	-6.50	-29.36	16.35	-0.56	0.577
Wen (2014)	-5.85	-19.65	7.94	-0.83	0.406
Archavlis (2013)	-14.62	-37.45	8.21	-1.26	0.209
Yang (2013)	-12.19	-36.09	11.71	-1.00	0.317
Harris (2011)	-11.83	-35.79	12.12	-0.97	0.333
Wang (2011)	-12.06	-35.54	11.41	-1.01	0.314
Yang (2011)	-10.09	-34.94	14.76	-0.80	0.426
Cho (2007)	-16.34	-38.89	6.21	-1.42	0.156

ODI: Oswestry Disability Index; VAS: Visual analogue scale

Table 3. Sensitivity Analysis (Cont'd)

First Author (Year)	Statistics with Study Removed				
	Points	Lower Limit	Upper Limit	Z Value	*P* Value
Length of hospital stay					
Ang (2015)	-3.18	-4.01	-2.34	-7.44	<0.001
Nerland (2015) - one	-3.22	-4.04	-2.39	-7.64	<0.001
Nerland (2015) - two	-3.18	-4.05	-2.31	-7.15	<0.001
Hu (2014)	-2.81	-3.55	-2.07	-7.49	<0.001
Wen (2014)	-2.96	-3.74	-2.19	-7.50	<0.001
Yang (2013)	-3.02	-3.83	-2.21	-7.29	<0.001
Harris (2011)	-3.26	-4.03	-2.49	-8.28	<0.001
Yang (2011)	-3.05	-3.82	-2.27	-7.70	<0.001
Yagi (2009)	-2.55	-3.19	-1.92	-7.91	<0.001
Cho (2007)	-3.00	-3.78	-2.22	-7.55	<0.001
Estimated intraoperative blood loss					
Luo (2015)	-198.65	-271.35	-125.94	-5.36	<0.001
Hu (2014)	-187.87	-287.84	-87.91	-3.68	<0.001
Singh (2014)	-182.86	-252.31	-113.41	-5.16	<0.001
Wen (2014)	-173.92	-240.37	-107.48	-5.13	<0.001
Archavlis (2013)	-197.61	-264.79	-130.44	-5.77	<0.001
Yang (2013)	-170.79	-238.07	-103.50	-4.97	<0.001
Harris (2011)	-195.21	-263.07	-127.35	-5.64	<0.001
Wang (2011)	-170.83	-238.25	-103.42	-4.97	<0.001
Yang (2011)	-207.61	-274.90	-140.33	-6.05	<0.001
Cho (2007)	-215.55	-281.97	-149.14	-6.36	<0.001
Events of dural tear					
Ang (2015)	0.80	0.43	1.51	-0.68	0.497
Nerland (2015)	1.48	0.65	3.39	0.93	0.354
Mobbs (2014)	0.87	0.47	1.64	-0.42	0.674
Wen (2014)	0.77	0.40	1.48	-0.78	0.433
Archavlis (2013)	0.87	0.46	1.64	-0.43	0.669
Harris (2011)	0.85	0.45	1.61	-0.50	0.616
Wang (2011)	0.95	0.48	1.86	-0.16	0.874
Yang (2011)	0.79	0.42	1.49	-0.72	0.471
Events of wound infection					
Nerland (2015)	0.36	0.10	1.23	-1.64	0.102
Wen (2014)	0.68	0.27	1.75	-0.79	0.428
Yang (2013)	0.67	0.28	1.60	-0.90	0.370
Wang (2011)	0.72	0.30	1.73	-0.74	0.462
Yang (2011)	0.67	0.28	1.59	-0.91	0.365
Cho (2007)	0.56	0.24	1.32	-1.33	0.185

ODI: Oswestry Disability Index; VAS: Visual analogue scale

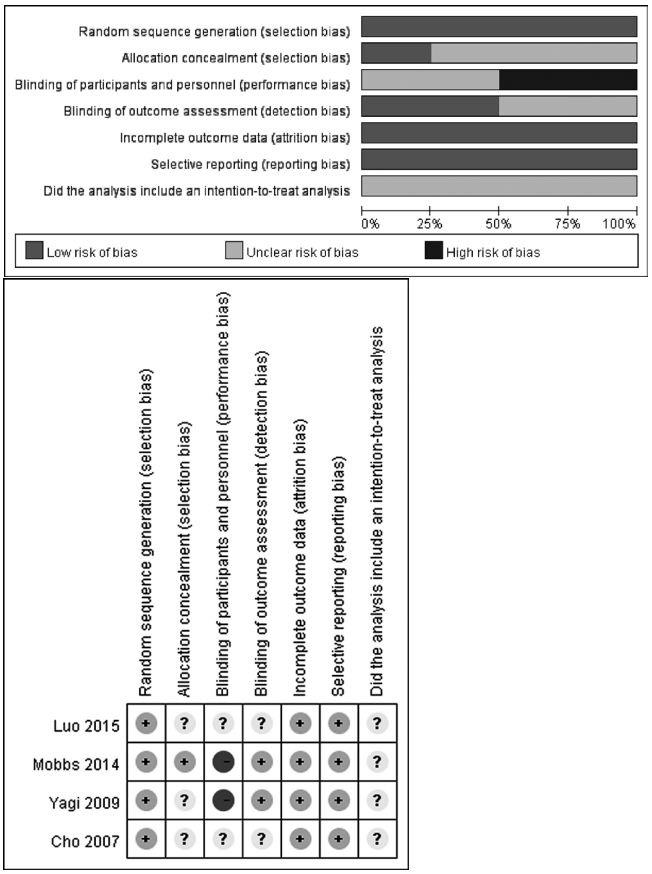

Fig. 5. Quality assessment.

studies showed blinding bias. This was expected as double blinding was difficult to perform due to the necessity of different surgical interventions. The risk of intention-to-treat analysis was unclear. Overall, the included studies had low risk for attrition and reporting bias, but high risk of performance bias (Fig. 5B).

Discussion

Although open laminectomy is the standard of care for treatment of lumbar stenosis, it may lead to adverse consequences, such as flexion instability, muscle weakness, and failed back surgery syndrome due to profound disruption of spine and surrounding muscle structures.[7-11] In recent years, there has been rapid development of the minimal access techniques for decompression and stabilisation of the lumbar spine. A number of potential benefits of this approach include smaller scars, decreased blood loss, reduced wound pain, and shorter hospital stays. These benefits, however, have to be carefully considered against possible shortcomings, such as a steep learning curve for doctors as well as high cost of equipment for implementation of MIS. The purpose of our meta-analysis study was to assess the clinical outcome, safety, and efficiency of MIS compared with open laminectomy in the treatment of lumbar stenosis. To our knowledge, this is the first meta-analysis on this topic.

Our results found no significant difference in ODI and operation time between MIS and conventional OS. However, MIS was associated with significantly better VAS for back pain, shorter length of hospital stay, and lower blood loss than conventional OS. Overall, subgroup analysis which compared MIS with TLIF or conventional decompression surgery showed similar results to the overall analysis. Exceptions included the findings that VAS for back pain was similar between MIS and conventional decompression surgery, and no difference in length of hospital stay was seen between groups who received MIS or TLIF. Additionally, rates of complications, such as dural tear and wound infection were similar between MIS and conventional surgery.

The findings are consistent with previous studies. Recent systematic review concluded that, based on the available literature, minimally invasive lumbar surgery for posterior lumbar decompression or fusion has similar rate of complications compared with OS.[32] The authors also noted the reduction of blood loss was less with MIS, while the length of hospital stay was not dependent on choice of surgical intervention.[32] Payer at al analysed 9 studies comparing the MIS and standard OS in the treatment of degenerative lumbar stenosis and found that both procedures produced similar outcomes for lumbar disc herniation, or transforaminal or posterior lumbar interbody fusions.[33] In addition, a number of studies demonstrated a significantly shorter hospital stay for the patients who underwent minimally invasive lumbar laminotomy.[30,34-36]

It was previously shown that MIS techniques may lead to higher rates of complications, such as dural tears, inadequate decompression,[10,37] and longer operation times.[38] However, our study showed no significant differences in the rates of dural tear, wound infection, and operation times between conventionally or MIS-treated patients. It is possible that minimal exposure of the spine during MIS can result in incomplete treatment and lead to higher recurrence of symptoms at later follow-up times.[39,40] Assessment of the outcomes at later time points will help to address this possibility and to more accurately estimate the cost-effectiveness of MIS, which depends on sustained clinical benefits over time.[41]

The major limitations of our study are the small number of included publications, varied sample sizes, and the design heterogeneity in the analysed trials. Only 4 studies were RCTs. The sample size in the Nerland et al study was significantly larger compared to other included studies, which may have potentially influenced the treatment effect estimates. Moreover, details of surgical interventions

differed between the studies. Of the 16 included studies, only 2 (Archavlis et al, 2013 and Hu et al, 2014) reported results of postoperative VAS within 5 days of surgery. In Archavlis et al, no difference between treatment groups at day 3 postsurgery was observed. However, Hu et al observed that the MIS group had significantly better VAS compared with OS group. Due to only 2 studies reporting postoperative VAS findings, we did not perform a meta-analysis for this outcome. Additional controlled studies with larger patients groups and longer follow-up times are warranted to confirm our conclusions.

Conclusion

Our results highlight that employment of MIS techniques can lead to clinical outcomes that are comparable to those of conventional OS. Additionally, MIS is associated with lower blood loss and shorter hospital stay, and therefore could reduce the overall cost of care for lumbar stenosis patients. Hence, MIS techniques should be considered as a primary treatment for qualifying patients with lumbar stenosis.

Acknowledgement

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Original Article

Safety and Efficacy of Chloral Hydrate Sedation in Paediatric Sedation for Ophthalmic Procedures

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Abstract

Introduction: Chloral hydrate (CH) sedation is routinely used in paediatric ophthalmic examination in Singapore as an alternative to examination under general anaesthesia. Despite CH's traditionally high success rates and relatively low rate of adverse events, there is little data on its safety and efficacy as a sedative for ophthalmic procedures in an Asian population. Materials and Methods: A retrospective chart review was performed, including children who underwent CH sedation at the Singapore National Eye Centre from January 2012 to January 2015. Participants were given an initial dose of CH and a top-up dose if required. Univariate and multivariate analyses were performed on data collected. Results: CH sedation was successful in 144 of 153 children (94.1%). Of the 20 (13.0%) who required a top-up dose, 4 failed to sedate. The mean sedation onset was 29.4 minutes (SD: 24.3) and mean sedation duration was 56.5 minutes (SD: 24.0), with more than a third lasting more than 1 hour. The age of children, rather than initial dose of CH, was more relevant in determining success of sedation. Children who were >6 years old were 20.3 times more likely to fail sedation than those aged <2 years. During sedation, depression in the heart rate and a transient reduction of oxygen saturation was documented. All children recovered well post-sedation. Conclusion: CH is a very useful sedative for paediatric ophthalmic procedures, especially in younger children. Children over 4 years old were more likely to fail sedation and require top-up doses. Alternative means of sedation may need to be considered in these cases.

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Key words: Adverse effects, Anaesthesia, Procedural sedation, Sedatives

Introduction

Sedation is often required to successfully conduct paediatric clinical ophthalmic examinations or diagnostic investigations when children are unable to cooperate due to anxiety or fear.[1] Chloral hydrate (CH) is commonly used for such situations. CH works by being metabolised into its pharmacologically active metabolite, trichloroethelene (TCE), which is postulated to work on the gamma-aminobutyric acid type A (GABAA) receptors in the central nervous system to achieve its sedative effects.[2] It can be orally administered, has high rates of success (88% to 100%) as a sedative and is relatively safe.[3] However, it has a bitter taste and has been associated with adverse effects including nausea, vomiting, respiratory depression, oxygen desaturation, paradoxical reaction, and rarely, deaths.[1,4-7] It has also been associated with carcinogenesis in animal studies.[8]

Use of CH in ophthalmology was first described in 1974 when it was used to conduct electroretinography in children.[9] Most studies have focused retrospectively on its safety and efficacy in dental and radiological procedures.[10] The few studies regarding CH sedation for ophthalmic procedures suggest it is safe and effective as a paediatric sedative due to low incidences of adverse events and high sedation success rates.[6]

Recently, there has been a push worldwide to improve the quality of healthcare and safety of patients. As such, there has been an increasing concern with the use of CH in the

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outpatient setting, given its variable efficacy, long half-life and adverse effects profile, especially since newer sedative agents (e.g. intranasal dexmedetomidine) have been found to be as effective with minimal cardiorespiratory effects.[4] The studies on CH thus far have focused on dental and radiological requirements, where the duration of sedation and invasiveness of procedures are greater and doses administered were consistently higher.[10] In the ophthalmic setting, CH sedation was used sparingly and only when a short but thorough examination of the ocular structures or fundus was required (e.g. in cases of leucocoria, suspected glaucoma, postoperatively after cornea, glaucoma or retina surgery, and for electrophysiology tests). In this study, we reviewed children who underwent CH sedation at the Singapore National Eye Centre (SNEC) from January 2012 to 2015 with the aim of determining the safety and efficacy of CH sedation for ophthalmic procedures using a range of CH doses in a predominantly Asian paediatric population.

Materials and Methods

A retrospective chart review was performed for all children who underwent CH sedation between January 2012 and January 2105 at SNEC. Suitable patients were identified through our sedation record and relevant data was collected by tracing all case notes and CH sedation record forms. Data gathered comprised demographic data including age, weight and gender, and sedation parameters such as sedation dosage, top-up dosage, time of administration, sedation onset, sedation duration, vitals every 15 minutes during sedation, sedation score and presence of adverse effects. This study was done as part of a clinical audit in preparation of a Joint Commission International (JCI) inspection.

Sedation Procedure

Sedation was performed with the supervision of trained nurses and ophthalmologists at the outpatient clinic. Patients were fasted for 3 hours prior to sedation. The ophthalmologist in charge assessed fitness for sedation; patients with unstable medical conditions, abnormal airway or respiratory disorders, degenerative neuromuscular disease, and patients on medications that may cause drowsiness such as antiepileptics or opiates were not sedated. Informed consent was obtained from parents or legal guardians before sedation. Baseline vital signs (heart rate [HR], blood oxygen levels and respiratory rate) were documented by nurses. A single dose of oral CH, ranging from 30 mg/kg to 75 mg/kg, was administered and if necessary, a top-up dose of less than half of the original dose was added. Once the children fell asleep, a pulse oximeter was used to monitor HR and blood oxygen levels continuously.

The clinic was fully equipped with resuscitation equipment and the support of trained personnel. Sedation score and vital signs were recorded before sedation, every 15 minutes during sedation till patients were fully awake and every 30 minutes post-procedure until the discharge criteria was met. We measured sedation using the Ramsey Sedation Scale – 1: when the child is anxious or restless or both; 2: when the child is cooperative, orientated and tranquil; 3: when the child responds to commands; 4: a brisk response to stimulus; 5: sluggish response to stimulus; and 6: no response to stimulus.[11] The procedures were performed when patients were adequately sedated. After arousal, patients were discharged only when they met the criteria of having vital signs within normal limits (O_2 level >90% or pulse rate >80 beats per minute), being conscious and alert, able to tolerate fluids and to sit or stand or walk according to their age.

Sedation success, need for a top-up dose and incidence of any adverse event during or post-sedation were measured. We defined sedation success as the achievement of adequate sedation for procedures to be performed, with a Ramsay scale of at least 4 (i.e. a brisk response to light glabellar tap or loud auditory stimulus).[11] This could have been achieved with a single dose or an additional top-up dose. Top-ups were considered if child was still awake 45 minutes after the medication was administered, especially if the child spat or vomited a sizeable amount of the medication.

Statistical Analysis

Continuous variables were reported with their mean, median, standard deviation (SD) and range, whereas categorical data were reported with their percentages. We ran statistical analyses on continuous variables using Student's t-test and on categorical data using Pearson's chi-square test. Variables with a P value <0.05 were deemed statistically significant.

Results

Patient Demographics

Over a 3-year period, 153 children received CH sedation; 62.1% were males, with a mean age of 2.4 years (SD: 1.7; age range, 1 month to 97 months) (Fig. 1). Most patients were Chinese (42.4%), followed by Indian (14.3%), Malay (4.6%) and patients of other races (Table 1).

Sedation Success and Failure

Of the 153 patients, 144 (94.1%) were successfully sedated. Twenty children (13.0%) required a top-up. Sedation failed in 9 children (5.9%), of which 4 failed despite top-ups (Table 2). Sedation was successful in 95.8%

Table 1. Demographics, Dose, Sedation Onset, Duration, and Baseline Vital Signs in Children of Different Age Groups

Variable	Total No. (n = 153*)	<2 Years Old (n = 69)	2 – 4 Years Old (n = 62)	>4 Years Old (n = 22)	*P* Value <2 vs 2 – 4 Years Old	*P* Value <2 vs >4 Years Old	*P* Value 2 – 4 vs >4 Years Old
Gender (Male, %)	95 (62.1%)	41 (59.4%)	41 (66.1%)	13 (59.1%)	0.428	0.487	0.554
Chinese (%)	65 (42.5%)	29 (42.0%)	29 (46.8%)	7 (31.8%)	0.277	0.602	0.218
Mean initial dose, mg/kg (SD)	49.5 (5.4)	48.7 (6.3)	50.2 (5.0)	50.1 (2.8)	0.159	0.338	0.944
Need to top-up (%)	20 (13.1%)	9 (13.0%)	4 (6.5%)	7 (31.8%)	0.277	0.116	0.002
Mean total dose, mg/kg (SD)	51.3 (7.5)	51.0 (9.2)	51.0 (5.7)	53.3 (6.0)	0.957	0.290	0.113
Sedation onset, minutes (SD)	29.4 (24.3)	22.8 (13.5)	28.4 (16.1)	58.8 (49.4)	0.035	<0.001	0.001
Sedation duration, minutes (SD)	56.5 (24.0)	57.0 (26.2)	56.9 (21.9)	53.5 (23.4)	0.982	0.620	0.582
Failed to sedate (%)	9 (5.9%)	2 (2.9%)	2 (3.2%)	5 (22.7%)	0.001	0.009	0.004
Baseline heart rate (SD)	109.3 (19.4)	120.0 (18.4)	100.6 (14.6)	101.0 (17.4)	<0.001	<0.001	0.839
Heart rate <80% of baseline during sedation	44 (32.8%)	20 (31.7%)	14 (25.9%)	10 (58.8%)	0.489	0.090	0.012
Oxygen saturation <95% during sedation	5 (3.7%)	4 (6.3%)	1 (1.9%)	0 (0%)	0.222	0.554	0.579
Baseline respiratory rate (SD)	25.5 (2.0)	26.0 (2.2)	25.3 (1.5)	24.7 (1.8)	0.039	0.011	0.117
Respiratory rate <90% of baseline during sedation	16 (11.9%)	9 (14.1%)	6 (11.1%)	1 (5.9%)	0.605	0.980	0.541

SD: Standard deviation

*Total number may not add up to 153 children for vital signs measurements as 10 patients failed to sedate and 10 patients were uncooperative and did not allow baseline measurements to be taken at onset.

of children weighing <15 kg compared to 87.8% in those weighing >15 kg ($P = 0.085$).

The initial and total doses given were similar in different age groups with a mean initial dose of 49.5 ± 5.4 mg/kg (range, 19.5 mg/kg to 60.8 mg/kg) (Table 1). Overall, 16 (10.5%), 111 (72.5%), 26 (17.0%) children received <45 mg/kg, 45 mg/kg to 50 mg/kg, and >55 mg/kg of CH, respectively. Logistic multivariate analysis suggested that the odds of sedation failure or requiring a top-up increased with age, and was 20.3 times more likely in children >6 years old than in those aged <2 years ($P = 0.010$) with initial dose used being less relevant ($P > 0.389$).

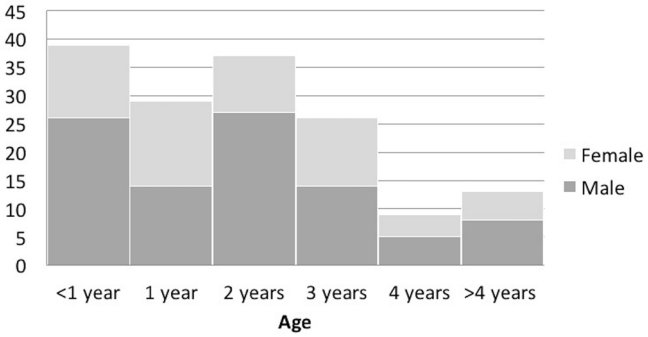

Fig. 1. Patient demographics (n = 153).

Table 2. Comparative Sedation Data

	Total (n = 153)	Success			Failure		
		Total (n = 144)	Without Top-up (n = 128)	After Top-up (n = 16)	Total (n = 9)	Despite Top-up (n = 4)	Without Top-up (n = 5)
Mean age, years (SD)	2.4 (1.7)	2.3 (1.6)	2.2 (1.4)	3.0 (2.4)	3.8 (2.5)	4.4 (3.7)	3.4 (2.0)
Mean weight, kg (SD)	12.1 (4.2)	11.9 (4.0)	11.8 (3.8)	12.5 (5.5)	15.3 (5.9)	14.6 (5.2)	15.9 (6.9)
Chinese	42.4%	43.1%	43.8%	37.5%	33.3%	75.0%	0%
Initial dose, mg/kg (SD)	49.5 (5.4)	49.8 (4.7)	49.7 (4.9)	50.4 (4.7)	45.2 (10.9)	41.6 (14.7)	48.2 (7.1)
Total dose, mg/kg (SD)	51.3 (7.5)	51.5 (7.3)	49.7 (4.9)	65.4 (8.6)	49.2 (10.5)	50.5 (15.0)	48.2 (7.1)

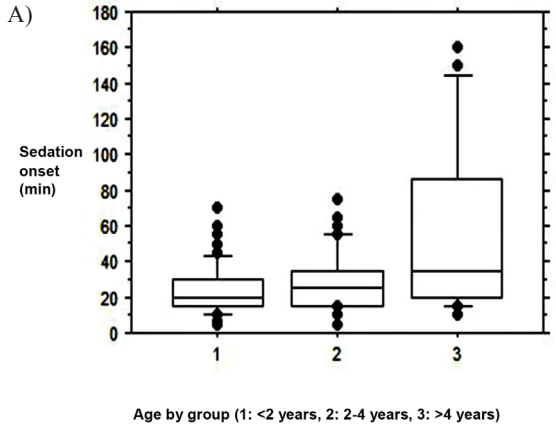

Fig. 2. A) Box plot of sedation onset and B) duration versus age.

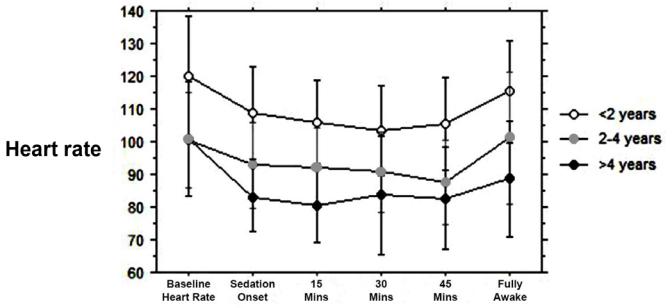

Fig. 3. Change in heart rate over time (line-chart).

Sedation Onset and Duration

The mean sedation onset for successful cases was 29.4 ± 24.3 minutes (range, 5 to 160 minutes). A total of 102 children (70.8%) were sedated within 30 minutes, and 93.0% within 1 hour. The mean sedation duration was 56.5 ± 24.0 minutes (range, 5 to 140 minutes). Ten children (6.9%) had a sedation onset of more than 1 hour while 52 children (36.1%) remained sedated for more than 1 hour. Those who remained sedated for >100 minutes were all below 3 years of age.

Univariate analysis suggested that older children took longer to sedate, but duration of sedation was similar across ages (Fig. 2). Multivariate analysis confirmed this (Table 3), and further suggested that duration of sedation was not affected by gender or initial dose used.

Change in Vital Signs

Baseline vitals were present in all but 10 children who resisted attempts to measure their vitals prior to sedation. In general, younger children had a higher baseline HR than older children (Table 1). A reduction in HR was noted at sedation onset, remained stable over the period of sedation, and returned to baseline on waking (Fig. 3). A total of 55.2% of children (n = 74) had a fall of HR >10 beats per minute from baseline, with children >4 years old having the greatest decrease in HR. However, none had HR that decreased below age-related normal ranges.[12]

Respiratory rate (RR) remained relatively stable throughout sedation across all age groups (Fig. 4). Measurements of oxygen saturations showed a transient reduction in oxygen saturation, which recovered by the 15-minute assessment with none requiring oxygen supplementation (Fig. 5). Only 1 of the 5 children whose oxygen saturations dropped below 95% had a baseline saturation of 94%; the rest had >95% baseline saturation. The lowest oxygen saturation encountered during sedation was 92%. Oxygen levels often improved after a readjustment of child's head position.

Table 3. Multivariate Analysis of Onset and Duration of Sedation

	Onset of Sedation -β	95% CI	*P* Value	Duration of Sedation β	95% CI	*P* Value
Male	-0.32	-7.78 to 7.13	0.932	-0.67	-9.15 to 7.81	0.876
Initial dose, mg/kg	-0.09	-0.83 to 0.63	0.791	-0.18	-1.01 to 0.65	0.668
Age	10.34	6.34 to 14.34	0.000	-0.10	-4.6 to 4.43	0.965

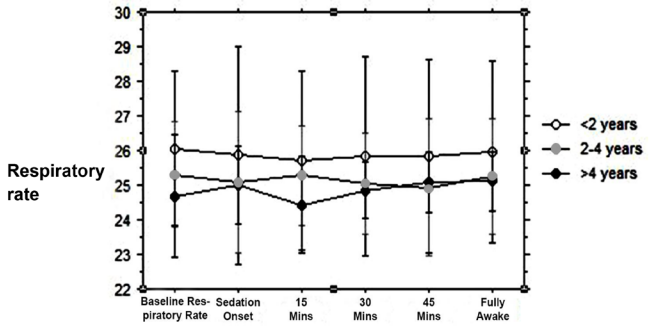

Fig. 4. Change in respiratory rate over time (line-chart).

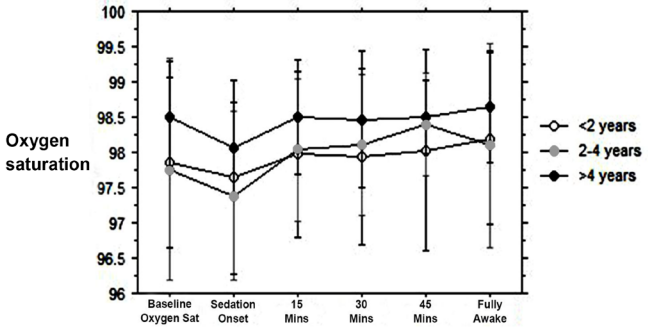

Fig. 5. Change in oxygen saturation over time (line-chart).

Other Effects

Six children (3.9%) vomited or spat out medication at the time of administration. Sedation was still successful after the vomiting/spitting out, except in 1 case where the child's parents decided not to proceed. No cases of paradoxical hyperactivity were noted.

Discussion

In this study, CH sedation for ophthalmic procedures was highly successful. Failure to sedate and need for top-up was more likely in older children, particularly in those more than 4 years old. We also noted minimal changes in vital signs and that all children recovered well from sedation. No other major adverse effects requiring hospitalisation or paradoxical hyperactivity were documented.

Efficacy

Our sedation success rate of 94.1% was similar to those of 96.7% and 97.9% cited in West et al[1] and Wilson et al[10], respectively. It was also within the 88% to 100% success ranges noted in older publications and in radiological and dental literature.[6,7,13] Variability in success rates may be partially due to patient selection and doses used (as high as 80 mg/kg to 100 mg/kg in some studies). In this study, we also noted that sedation in children >6 years old were 20.3 times more likely to fail or require top-up doses than those aged <2 years. This is consistent with existing literature, where failure rates were higher in those aged 48 months and above.[1,14] Our findings are also in line with the current National Institute for Health and Care Excellence (NICE) guidelines, which recommends CH as an agent for mild to moderate sedation during painless procedures for children under 15 kg; our success rate for sedation for those <15 kg was 95.8%, compared to 87.8% in those >15 kg.[15] Possible explanations include older children metabolising the drug faster, as the half-life of CH does decrease with age,[16] and older children being more aware and anxious, and thus, more likely to resist the effect of sedation. Hence, older children may benefit from alternative means of sedation.

Although the approximate time for sedation onset and duration was 30 minutes and 60 minutes, respectively, the range of onset and duration was quite wide and unpredictable. Jaafar and Kazi[7] reported a mean sedation onset of 25 minutes and sedation duration of 60 minutes using 100 mg/kg of CH for the first 10 kg and 50 mg/kg, respectively, for every additional kg while West et al[1] quoted 28.8 minutes and 53.4 minutes on 80 mg/kg of CH. Similar to other studies, these sedation durations appear to be independent of doses used.[17] In this study, 6.9% had a sedation onset of more than 1 hour, while 36.1% remained sedated for more than 1 hour. Those who remained sedated for >100 minutes were all younger than 3 years old. Other studies also noted delayed recovery in children <1 years old, and prolonged sedation >2 hours in 3.3%.[18] The prolonged effect of CH in younger children may be due to differences in CH metabolism with age.

Safety

CH is absorbed by the gastrointestinal tract and reaches peak serum concentrations in 30 to 60 minutes, and later metabolised to TCE by alcohol dehydrogenase in the liver. TCE causes the sedative effect of CH and has a half-life of approximately 8 to 12 hours.[5] The long half-life of TCE is especially of concern as it has been shown to be 3 to 4 times longer in neonates and infants than in older children.[16] Mayers et al also demonstrated that TCE half-life was 27.8 hours in term infants and 9.67 hours in older children, with peak TCE concentrations decreasing with age. This may explain the prolonged sedation and delayed recovery in younger children and the higher failure rates in older children.[19]

Although CH has a relatively good safety profile, its long half-life means that it may still have a sedative effect even after discharge.[18] Post-discharge side effects include

sleepiness lasting >8 hours in 11% of children, unsteadiness in 48% and hyperactivity in 29%.[19] Nordt et al[5] has also documented 3 cases of major adverse events, including 2 incidences of over-sedation and 1 death. One was the result of an accidental overdose, while the other child had pre-existing neurological problems. The fatal episode occurred after discharge with prolonged sedation. These further emphasise the need for strict sedation guidelines that account for pre-existing medical problems, monitoring under professional supervision and proper discharge counselling of parents.

We also found that CH sedation resulted in general depression of HR within normal age-related parameters and a transient reduction in oxygen saturation. In contrast, respiratory rates remained relatively stable over time.

Under normal physiological conditions, HR often slows during sleep.[20] In our study, HR decreased at the onset of sedation and plateaued, reverting to baseline on awakening, and none were outside of normal age-related parameters.[14] About 32.8% of children had a fall of HR of >20% during sedation, with the children aged >4 years recording greater falls. This may be due to the older children being more aware of the situation and having a higher baseline HR due to anxiety or fear, thus having a greater fall in HR during sedation.[21] Our findings corresponded to Heistein et al,[18] who found that 24% of patients had a greater than 20% departure from their baseline HRs, of which only 1.7% had a drop lower than the normal range for their age. Intervention was also not needed in our study for the transient bradycardia recorded, suggesting that reductions in HR did not impair protective airway reflexes.[18]

Of more concern was the transient fall of oxygen saturation at the time of sedation onset, although oxygen saturation of <95% was noted in 3.7% of the children. In almost all cases, oxygen saturations had returned to baseline by the 15-minute assessment period. Vade et al[22] reported a higher rate of hypoxia, with departure of oxygen saturation <95% in 9% of the children, which spontaneously recovered by 5 to 10 minutes. Other studies had lower published rates of hypoxaemia of between 0.99% and 0.26%, which were possibly due to their larger sample size and children who were only either ASA class 1 (healthy) or 2 (mild systemic disease).[1,10] The transient fall in oxygen saturation may reflect the presence of respiratory suppression or obstruction of the airway. In most cases, proper positioning of the child could rectify this. We suggest maintaining close vigilance with a readiness to act (e.g. by suctioning of airway or oxygen supplementation) as necessary.

The other most common adverse effect was vomiting or spitting out medication. Our rates of vomiting/spitting out (3.9%) were in the range of other studies (0.53% to 20%).[1,7] Other adverse effects, including paradoxical reaction, airway obstruction, apnoea, hypotension, and rarely, cardiac arrhythmias and death, were not noted in our study.[16] Overall, CH was demonstrated to be a safe sedative with low rates of gastrointestinal irritation and transient decreases in HR and oxygen saturation that recovered without medical intervention. Surprisingly, we did not have any cases of paradoxical reaction or excess irritability despite it being a common adverse effect of CH sedation, with rates of 1.5% to 6.3%.[1] This might be a limitation of the study being retrospective, with inadequate accounting of certain events or agitation being subjectively dependent on observer interpretation.

Strengths and Limitations

Other limitations of the study include the lack of evaluation of blood pressure, post-discharge events, such as re-admission to hospital or persistent excessive drowsiness, and history of multiple sedations, as these were not included in our protocol forms. Another limiting factor was that standard dosing was not employed, as different consultants adopted varying dosing regimens, although majority administered an initial dose of approximately 50 mg/kg. However, the strengths of the study lie in its consistent recording of sedation cases with a standardised proforma, with well documented adverse effects. We also used specified validated scales (Ramsay Sedation Scale) to determine adequate sedation.

Conclusion

CH is a very useful sedative for paediatric ophthalmic examinations, especially in younger children. The age of children, rather than initial dose of CH, was more relevant in determining success of sedation in our predominantly Asian population. Children over 4 years of age were more likely to fail sedation and require top-up doses. Alternative means of sedation may need to be considered in these cases. To ensure patient safety, continuous monitoring during sedation is useful, and parents need to be made aware of the side effects, long half-life and care required in the post-sedation period. Adequate education and training of doctors and nurses is needed to ensure awareness of their individual roles and responsibilities, and ability to react in case of emergency.

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Original Article

Hearing Loss amongst the Elderly in a Southeast Asian Population – A Community-based Study

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Abstract

Introduction: The aim of this study was to determine the prevalence of hearing loss amongst the elderly population attending community services in Singapore. The usefulness of the Hearing Handicap Inventory for the Elderly Screening version (HHIE-S) in detecting hearing loss was also investigated. Materials and Methods: Pure-tone audiometry was carried out on a randomly recruited cohort of people (n = 338) over 60 years old and who were attending rehabilitation and social day care services for senior citizens at St Luke's Elder Care centres located throughout the city. Prior to the hearing test, subjects were administered the HHIE-S questionnaire, which was translated into the language they were most conversant in. Results: The study cohort showed mean pure-tone average at speech frequencies (0.5, 1, 2 and 4 kHz; 4-frequency average hearing level [4FA HL]) of the subjects' better hearing ear that has worsened with age. The percentage of the elderly with disabling hearing impairment (4FA >40 dB HL) was 9.1% (60 to 69 years old), 22.0% (70 to 79 years old), 35.7% (80 years old and above). Across all age groups, males had significantly poorer thresholds at 4 kHz than females. When adjusted for the demographic profile of the country, the prevalence of hearing loss (4FA >25 dB HL) and disabling hearing impairment (4FA >40 dB HL) amongst the elderly in Singapore was 63.7% and 16.2%, respectively. We estimate that there are currently 422,000 elderly with hearing loss greater than 25dB HL and over 100,000 elderly with disabling hearing loss of over 40 dB HL. Of subjects with a disabling hearing impairment, only 7.5% used hearing aids. The use of self-reporting HHIE-S showed poor sensitivity in detecting hearing loss of various severities amongst the elderly. Conclusion: These data provide estimates of the prevalence and severity of hearing loss in older persons in Singapore and suggest that more can be done to help the elderly recognise, acknowledge and address hearing loss in the country.

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Key words: Audiology, Epidemiology, Geriatric, Hearing Aids, Singapore

Introduction

Presbycusis, or age-related hearing loss, is a common condition among the elderly and a burgeoning problem in societies with ageing populations such as Singapore. In the last 2 decades, the percentage of the elderly (aged 60 years and above) in Singapore's resident population has risen from 9.7% in 1995 to 17.9% in 2015.[1] The increase in life expectancy due to improvements in healthcare and standard of living means that there is a growing number of people with chronic conditions such as presbycusis. Presbycusis can impact quality of life by impairing communication, leading to poorer psychosocial functioning.[2] Additionally, epidemiologic research in the United States (US) has found an association between presbycusis and dementia.[3] This growing burden of presbycusis in the elderly is of concern, and it is imperative that countries facing ageing populations find ways to respond to these challenges.

Amongst Singapore's elderly population, there is only 1 published study carried out at a public hospital in 2004 which found that among 63 elderly patients of the geriatric medicine unit, 52 (83%) had hearing impairment worse than 30 dB HL.[4] There is no study that looks at hearing

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loss in the whole elderly population at a larger scale. Thus, the first aim of this study was to estimate the prevalence of hearing loss among the elderly in Singapore from a larger, non-hospital setting.

Standardised audiometric assessment is largely considered the gold standard in determining hearing loss in individuals. In prevalence studies however, standard testing may be difficult to carry out on a large scale, due to logistical and financial reasons. Another method utilised in epidemiological studies of disease prevalence is the use of self-report measures. Self-report measures, often in the form of questionnaires, can be reliable indicators of handicap. They are also quick and inexpensive to administer to a large group of study participants. The Hearing Handicap Inventory for the Elderly: Screening version (HHIE-S)[5,6] is one such instrument that assesses hearing loss. This questionnaire is a shortened version of the HHIE, and contains 10 questions regarding the effects of hearing impairment on emotional and social adjustments. The questionnaire has been shown to be a robust screening tool[7-9] in identifying elderly people who might benefit from audiological intervention. It has also been translated and used in different culture groups and countries.[10-13] In Singapore, the Health Promotion Board introduced the Functional Screening for Older Adults in the Community, a community health programme to detect and manage functional decline in the elderly population. As part of the screening protocol, the HHIE-S is used together with a Single Global Screening Question, "Do you or your family think that you may have hearing loss?" and audioscope testing to detect hearing loss in the elderly population.[14] However, the robustness of the HHIE-S has yet to be validated in the local population. The second aim of this study was to examine the sensitivity and specificity of this questionnaire in detecting hearing loss among the Singaporean elderly population.

Materials and Methods

Study Setting

St Luke's ElderCare Ltd is a non-profit organisation which provides rehabilitation and day care services for senior citizens. Since 2011, the organisation has been running 10 geographically dispersed centres across Singapore, with a diverse client pool of 1200 senior citizens. These clients live in their own homes but attend activities organised by the centres. The demographics of these clients form a representative sample of the elderly population in Singapore. The study was part of a community project organised by Temasek Polytechnic's School of Engineering and St Luke's ElderCare that offered hearing tests to senior citizens served by the respective ElderCare centres.

Participants

Nine out of 10 St Luke's ElderCare centres participated in the project. One centre (St Luke's Golden Years Centre) declined to participate. Written informed consent was obtained from all participants and the purpose of the study was explained to them. Participants (or their caregivers) had to fill in a form which screened for factors that might hinder their ability to provide accurate information, such as clinical dementia, neurological diseases or an inability to understand instructions. Individuals with any of the above conditions were excluded from the study. Only participants aged 60 years and above on the day of the hearing test were included in prevalence results analysis. The study was carried out over 2 days and participants consisted of the elderly who were attending the ElderCare centres during the study period.

Procedure

Pure-Tone Audiometry

Pure-tone audiometry was conducted on each participant using 3 Siemens SD28 diagnostic audiometers. The audiometers had undergone acoustic calibration by an external vendor 1 month prior to the study to ensure that the accuracy of the audiometers are within the tolerances permitted by American Standard Specification for Audiometers, S3.6-1969. As soundproof booths were not available at the centres, EARTONE 3A insert earphones were used for testing and were covered by 3M Peltor supra-aural earmuffs to attenuate ambient noise. This method allows for accurate threshold determination down to 0dB HL for 125-8000 Hz,[15] provided that ambient noise is not more than 40 dBA. The hearing tests were carried out in a quiet room and an Integrating Class 1 sound level meter (Model 1900; 3M Quest Technologies, Wisconsin, USA) was used to ensure that the ambient noise level was less than 40 dBA. The tests were performed by 3 students from Temasek Polytechnic, who had completed training equivalent to the Ministry of Manpower-accredited basic industrial audiometry course. The audiometers' proper functions were confirmed at the start of each day before audiometry was carried out. Air conduction thresholds were obtained for both ears at 0.5, 1, 2, and 4 kHz. These 4 frequencies were chosen as they covered the range of speech sounds. The average of the thresholds at these 4 frequencies was then calculated for each ear, and the better hearing ear (the ear with the lower average thresholds) was chosen for the final analysis. The average threshold for 0.5, 1, 2 and 4 kHz in the better hearing ear is referred to as the 4-frequency average (4FA).

Hearing levels of 25 dB and 40 dB are often used as screening criteria for mild and moderate hearing losses.[16] For the purposes of this analysis, we defined hearing

Table 1. Breakdown of Study Subjects by Centre Location

No.	ElderCare Centre (n = 338)	Male (n = 125)	Female (n = 213)	Min. Age (Years)	Max. Age (Years)
1	Serangoon	21	44	60	90
2	Yishun	8	24	60	90
3	Bukit Timah	3	15	61	88
4	Hougang	19	34	61	91
5	Tampines	26	37	61	94
6	Ayer Rajah	5	8	63	81
7	Jurong East	12	20	63	96
8	Whampoa	15	11	61	96
9	Telok Blangah	16	20	61	93

Table 2. Comparison between Study Subjects and Target Population

Age (Years)	*P* Value		Population		*P* Value for χ^2 Test
	For χ^2 Test (n = 338)	%	No. ('000)	%	
60 – 64					
Male	15	41.7%	110.2	49.6%	0.87
Female	21	58.3%	111.9	50.4%	
65 – 69					
Male	12	40.0%	70.5	48.4%	0.87
Female	18	60.0%	75.3	51.6%	
70 – 74					
Male	22	40.0%	48.7	46.0%	0.90
Female	33	60.0%	57.1	54.0%	
75 – 79					
Male	24	38.1%	31.2	44.1%	0.90
Female	39	61.9%	39.5	55.9%	
80 – 84					
Male	32	38.1%	18.6	40.3%	0.96
Female	52	61.9%	27.6	59.7%	
≥85					
Male	20	28.6%	11.9	33.1%	0.92
Female	50	71.4%	24.1	66.9%	

impairment as having a 4FA of >25 dB HL. Disabling hearing impairment was defined as having a 4FA of greater or equal to 40 dB HL.

Questionnaire

The questionnaire administered consisted of 2 parts and was administered verbally. The first contained questions from the HHIE-S. Developed as a diagnostic tool to identify older people with hearing difficulties, the HHIE-S consists of 10 questions designed to assess perceived emotional and social problems associated with impaired hearing (e.g. frustration, embarrassment or difficulty in certain situations). One of 3 responses ("yes", "sometimes" or "no") was recorded for each question and scored as 4, 2, or 0, respectively. Missing values were excluded and scores from the 10 questions were totalled for a minimum score of 0 and a maximum score of 40. According to guidelines by the American Speech-Language Hearing Association (ASHA), scores of >8 indicate the presence of a hearing handicap.[15] This cutoff point was used to validate the usefulness of the HHIE-S instrument in predicting hearing loss measured using pure-tone audiometry measurements. For non-English speakers, the HHIE was translated to Chinese[11] as well as various Chinese dialects and Malay. The second part of the questionnaire pertained to the use of hearing aids.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) Version 12.0 for Windows (SPSS Inc., 2003), with a *P* value of <0.05 taken to be significant for all tests. In addition to descriptive statistics, analysis of variance (ANOVA) was used to analyse the results of the pure-tone audiometry. The screening performance of the HHIE-S was separately assessed for sensitivity, specificity, positive and negative predictive values. The difference between measured and estimated prevalence was also obtained.

Results

A total of 366 people aged above 60 participated in the hearing tests at the various centres; 28 of them were excluded either due to suspected or confirmed clinical dementia, or neurological disorders. A breakdown of the 338 subjects included in the final analysis is shown in Table 1.

Comparison of Study Cohort to Local Population

A comparison of this study cohort to the local population over 60 years of age is shown in Table 2. The proportion of males and females in the study cohort was not significantly different to that of the local population for all age groups.

Prevalence of Hearing Loss

The 4FA of the participants stratified by age and gender is shown in Table 3. The mean 4FA for the whole cohort ranged from 20.5 dB HL to 52.4 dB HL. One-way ANOVA showed

Table 3. Pure-Tone Threshold Average (4FA) Stratified by Age Groups and Sex

Age (Years)	n = 338	4FA (dB HL)			
		Mean	SD	Min.	Max.
60 – 64					
Male	15	29.7	15.1	13.75	62.5
Female	21	20.5	9.6	5.0	42.5
Total	50.1	24.3	12.8	5.0	62.5
65 – 69					
Male	12	32.9	9.8	21.25	55.0
Female	18	23.4	8.4	8.75	38.8
Total	56.3	27.2	10.0	8.75	55.0
70 – 74					
Male	22	37.6	14.8	15	65.0
Female	33	35.7	12.6	15.0	66.3
Total	73.3	36.5	13.4	15.0	66.3
75 – 79					
Male	24	40.7	16.8	21.25	82.5
Female	39	37.5	13.5	8.75	73.8
Total	78.2	38.7	14.8	8.75	82.5
80 – 84					
Male	32	45.0	15.7	20	101.3
Female	52	41.2	15.5	21.3	90.0
Total	86.2	42.6	15.6	20.0	101.3
≥85					
Male	20	52.4	13.0	22.5	83.8
Female	50	45.9	11.4	23.75	71.3
Total	98.2	47.7	12.1	22.5	83.8
All					
Male	238.3	41.1	16.1	13.75	101.3
Female	204.1	37.2	15.0	5	90.0
Total	78.3	38.6	15.5	5	101.3

4FA: Four-frequency average of 0.5, 1, 2 and 4 kHz; SD: Standard deviation

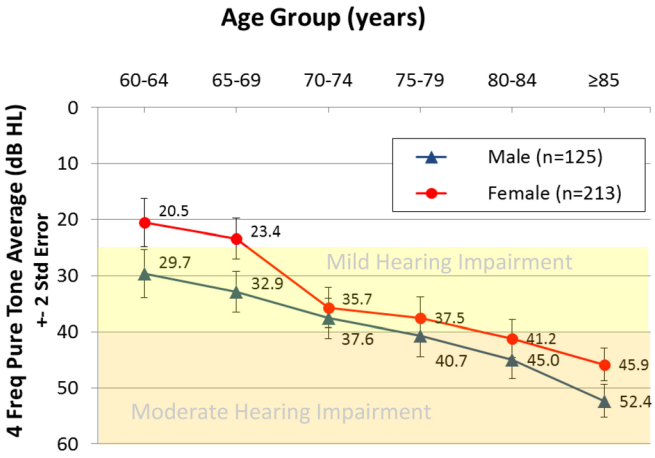

Fig. 1. The difference in 4FA thresholds between genders at various age groups.

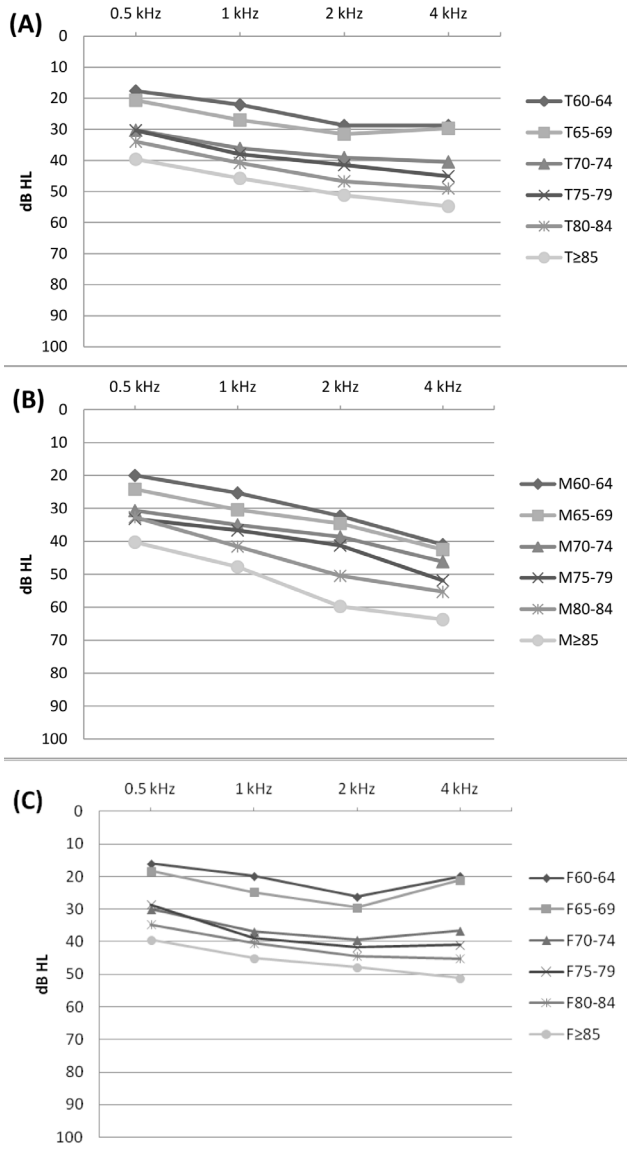

Fig. 2. Average threshold at each frequency, stratified by age groups, for A) total study cohort, B) males, and C) females.

that the mean hearing thresholds increased significantly with age in the total study cohort, as well as for both males and females. The mean hearing thresholds for male subjects was also poorer than that of female subjects. This difference is significant in the all age groups (with the exception of the 70 to 74 age group). The mean 4FA thresholds between genders at various age groups are illustrated in Figure 1.

Table 4 shows the mean pure-tone thresholds for each of the 4 frequencies, grouped by gender and age. At 4 kHz, the male subjects had significantly higher thresholds than female subjects (P <0.0001). There was no statistically significant difference in mean thresholds between the genders at other frequencies. As illustrated in Figure 2, the

Table 4. Comparison of Mean Pure-Tone Thresholds (dB HL) in the Better Ear for Males, Females and Total Subjects

Age (years)	n = 338	0.5 kHz			1 kHz			2 kHz			4 kHz		
		Mean	SD	*P* Value	Mean	SD	*P* Value	Mean	SD	*P* Value	Mean	SD	*P* Value
60 – 64													
Male	15	20.0	15.4	0.210	25.3	11.7	0.121	32.3	18.0	0.226	41.0	28.7	0.010*
Female	21	16.0	10.3		19.8	9.3		26.2	11.9		20.0	17.7	
Total	36	17.6	9.4		22.1	10.6		28.8	14.9		28.8	24.9	
65 – 69													
Male	12	24.2	9.7	0.108	30.4	10.5	0.151	34.6	13.2	0.232	42.5	12.3	0.001*
Female	18	18.3	9.2		24.7	10.2		29.4	9.8		21.1	18.3	
Total	30	20.7	9.7		27.0	10.6		31.5	11.4		29.7	19.2	
70 – 74													
Male	22	30.7	17.7	0.875	35.0	15.1	0.643	38.6	16.0	0.849	46.1	18.8	0.065
Female	33	30.0	14.3		36.8	13.5		39.4	13.2		36.7	17.9	
Total	55	30.3	15.6		36.1	14.1		39.1	14.2		40.5	18.7	
75 – 79													
Male	24	33.1	18.4	0.269	36.7	17.5	0.605	41.3	18.7	0.922	51.9	18.3	0.018*
Female	39	28.6	13.8		38.8	15.3		41.7	14.8		40.9	16.7	
Total	63	30.3	15.7		38.0	16.1		41.5	16.3		45.1	18.0	
80 – 84													
Male	32	32.7	12.8	0.551	41.6	15.4	0.749	50.5	20.6	0.166	55.3	21.0	0.021*
Female	52	34.7	16.6		40.4	16.9		44.4	18.4		45.1	18.0	
Total	84	33.9	15.2		40.8	16.3		46.7	19.4		49.0	19.7	
≥85													
Male	20	40.3	14.5	0.811	47.8	12.0	0.405	59.8	21.2	0.008*	63.8	14.3	0.001*
Female	50	39.4	13.0		45.0	12.6		47.8	14.1		51.2	13.4	
Total	70	39.6	13.3		45.8	12.4		51.2	17.2		54.8	14.7	
All													
Male	125	31.3	15.4	0.753	37.4	15.7	0.927	44.4	20.4	0.080	51.4	20.6	0.000*
Female	213	30.7	15.6		37.3	15.9		40.9	16.2		40.0	19.6	
Total	338	30.9	15.5		37.3	15.8		42.2	17.9		44.2	20.7	

SD: Standard deviation

*Indicates statistically significant difference between the mean hearing thresholds of males and females within each category.

male participants of this study cohort showed a worsening of thresholds with increasing frequency, a trend which was not observed in the female participants.

The prevalence of hearing loss in the study cohort, stratified by age groups, is shown in Table 5. Overall, the prevalence of each category of hearing loss increased with age. The percentage of subjects with a hearing impairment (4FA >25 dB HL) was 48.5% for subjects aged 60 to 69 years, 82.2% for subjects aged 70 to 79 years and 93.5% for subjects aged 80 years and above. The percentage with a disabling hearing impairment (4FA >40 dB HL) for subjects aged 60 to 69 years, 70 to 79 years and above 80 years were 9.1%, 22.0% and 35.7%, respectively. Among subjects with a disabling hearing impairment, only 7.5% (10 out of 133 subjects) used hearing aids.

After adjusting for the demographic profile of the population, the prevalence of hearing loss (4FA >25 dB HL) and disabling hearing impairment (4FA >40 dB HL) among Singapore residents aged 60 and older was found to be 63.7% and 16.2%, respectively. Although there was a larger cohort of over 80-year-olds in our study than the general population, it is clear from our study that there is a significant hearing impairment problem in our elderly, even for those aged below 80. For example, just the group of 70 to 79 year olds alone had a 82.2% rate of hearing loss >25 dB and 22% rate of hearing loss >40 dB.

Table 5. Prevalence of Hearing Loss amongst the Elderly in Singapore

Age (Years)	% of Singapore's Elderly Population (a)	No. of Subjects Screened	Hearing Loss 4FA >25 dB HL		Disabling HL 4FA >40 dB HL		Marked HL 4FA >60 dB HL	
			No. of Subjects	Prevalence (b)	No. of Subjects	Prevalence (b)	No. of Subjects	Prevalence (b)
60 – 69	59.22%	66	32	48.5%	6	9.1%	2	3.0%
70 – 79	27.61%	118	97	82.2%	26	22.0%	7	5.9%
>80	13.16%	154	144	93.5%	55	35.7%	15	9.7%
All		338	273	80.8%	132	39.1%	30	8.9%
	Estimated National Prevalence = Σ(ai)x(bi)		63.7%		16.2%		4.7%	
	Estimated Number of Elderly		422,547		107,222		31,265	

4FA: Four-frequency average of 0.5, 1, 2 and 4 kHz

HHIE-S

The findings of the HHIE-S are summarised in Table 6, which shows the performance of each tool in detecting any hearing loss (4FA >25 dB), disabling hearing impairment (4FA >40 dB HL) and marked hearing impairment (4FA >60 dB) in the study cohort. In summary, the HHIE-S was found to be a poor predictor of hearing loss. However, the HHIE was a good predictor of hearing aid use (Table 7).

Discussion

Across the world, the prevalence of hearing loss in the elderly varies depending on the country, sample size, age definition of elderly and the audiometric criteria for hearing loss employed. The type of society one lives in also affects hearing loss, as industrialised societies have been shown to accelerate hearing loss with age compared to agrarian societies.[17,18] Such differences make the rates of hearing loss somewhat difficult to compare. Nevertheless, it is clear that across the world, a significant proportion of elderly people suffer from hearing loss. Table 8 displays the estimated prevalence of hearing loss for several different studies around the world.

Our study attempted to estimate the prevalence of hearing loss amongst the elderly population in Singapore. Based on the randomly-recruited cohort of the elderly living outside institutionalised care, a high percentage of them had some form of hearing impairment. When adjusted for the demographic profile of the country, the prevalence of hearing loss (4FA >25 dB HL) and disabling hearing impairment (4FA >40 dB HL) amongst the elderly in Singapore was 63.7% and 16.2%, respectively.

Table 6. Sensitivity, Specificity, PPV and NPV Values of the HHIE-S Questionnaire in Predicting Hearing Loss

Measured Hearing Impairment (Audiometry)	Hearing Loss PTA >25 dB HL	Disabling Hearing Loss PTA >40 dB HL	Marked Hearing Loss PTA >60 dB HL
Quantity (%)	273 (80.8%)	132 (39.1%)	30 (8.9%)
HHIE-S (≤8 or >8)			
PPV	94.3%	37.3%	10.1%
NPV	25.4%	77.1%	96.5%
Sensitivity	36.6%	47.7%	63.3%
Specificity	90.8%	68.6%	64.0%

HHIE-S: Hearing Handicap Inventory for the Elderly Screening version (HHIE-S); NPV: Negative predictive value; PTA: Pure-tone average; PPV: Positive predictive value

Table 7. Sensitivity, Specificity, PPV and NPV Values of the HHIE-S Questionnaire in Predicting Hearing Aid Use

	Wearing Hearing Aid (n = 132)
Quantity (%)	10 (7.5%)
HHIE-S (≤8 or >8)	
PPV	13%
NPV	97%
Sensitivity	80%
Specificity	56%

HHIE-S: Hearing Handicap Inventory for the Elderly Screening version (HHIE-S); NPV: Negative predictive value; PPV: Positive predictive value

Table 8. The Prevalence of Hearing Loss in the Elderly in Different Countries

Authors	Year	Country	Sample	n	Age Criteria (Years)	Frequencies (kHz) Measured	PTA Criteria	Percentage of Hearing Loss (>25 dB HL)	Percentage of Disabling Hearing Loss (>40 dB HL)
Gates GA et al*	1990	United States of America	Framingham Cohort	1662	63 – 95	0.5, 1, 2, 3	Better ear	42%	-
Lin FR et al†	2011	United States of America	National Health and Nutritional Exam Survey 2005 – 2006	717	48 – 92	0.5, 1, 2, 4	Better ear	44.80%	16.50%
Sindhusake D et al‡	2000	Australia	Blue Mountains	2015	55 – 100	0.5, 1, 2, 4	Better ear	39.10%	13.40%
Davis A§	1995	United Kingdom	National Study of Hearing (1980s)	2663	65 – 74	0.5, 1, 2, 4	Better ear	60%* (>20 dB)	20%* (>35 dB)
Hong JW et al‖	2015	Korea	2010 – 2012 Korea National Health and Nutrition Exam Survey	3562	>65	0.5, 1, 2, 3, 4, 6	Better ear	69.70%	35.1
Rosdina A et al¶	2010	Malaysia	Patients attending a primary care facility	111	>60	0.25, 0.5, 1, 2, 4	Better ear	36.90%	10.80%
Chang HP et al#	2007	Taiwan	Randomly-recruited cohort in Taipei	1221	>65	0.5, 1, 2, 4	Better ear	99.00%	52.70%
Lee GJC et al**	2017	Singapore	The elderly attending community aged care services	338	>60	0.5, 1, 2, 4	Better ear	63.70%	16.20%

PTA: Pure-tone audiometry

*Gates GA, Cooper JC Jr, Kannel WB, Miller NJ. Hearing in the elderly: the Framingham cohort, 1983-1985. Part I. Basic audiometric test results. Ear Hear 1990;11:247-56.

†Lin FR, Thorpe R, Gordon-Salant S, Ferrucci L. Hearing loss prevalence and risk factors among older adults in the United States. J Gerontol A Biol Sci Med Sci 2011;66:582-90.

‡Sindhusake D, Mitchell P, Smith W, Golding M, Newall P, Hartley D, et al. Validation of self-reported hearing loss. The Blue Mountains Hearing Study. Int J Epidemiol 2001;30:1371-8.

§Davis A. Hearing in adults: the prevalence and distribution of hearing impairment and reported hearing disability in the MRC Institute of Hearing Research's National Study of Hearing. London: Whurr Publishers Limited; 1995.

‖Hong JW, Jeon JH, Ku CR, Noh JH, Yoo HJ, Kim DJ. The prevalence and factors associated with hearing impairment in the Korean adults: the 2010-2012 Korea National Health and Nutrition Examination Survey (observational study). Medicine (Baltimore) 2015;94:e611.

¶Rosdina A, Leelavathi M, Zaitun A, Lee V, Azimah M, Majmin Sh, et al. Self reported hearing loss among elderly Malaysians. Malays Fam Physician 2010;5:91-4.

#Chang HP, Chou P. Presbycusis among older Chinese people in Taipei, Taiwan: a community-based study. Int J Audiol 2007;46:738-45.

**Lee GJC, Danker AN, Wong YH, Lim MY. Hearing loss amongst the elderly in a Southeast Asian population – A community-based study. Ann Acad Med Singapore 2017;46:145-54.

When compared to other large scale epidemiological studies done around the world, the local findings for the measured prevalence of hearing loss (4FA >25 dB HL) was higher than the US and Australia but lower than that of the Asian countries of Korea and Taiwan.

When we compared the prevalence of hearing loss >40 dB HL, our estimates of about 16.2% was quite consistent with the findings of other large scale studies carried out in developed countries (Table 8). When an individual's pure-tone average (PTA) is greater than 40 dB HL, his/her hearing is outside the audible range of some speech sounds. Such a hearing loss is significant enough to impact day-to-day communication. The World Health Organization (WHO) termed PTA >40dB HL as disabling hearing loss. In 2012, WHO released estimates on the magnitude of disabling hearing loss among the elderly aged 65 years and above based on 42 population-based studies.[19] Their estimates ranged from 32.8% for global average and 18.4% for high income nations. The prevalence found in our study puts us at the lower end of the range.

To put into perspective the magnitude of the health problem affecting our nation, based on the recent population data of Singapore, we estimated that there are currently 422,000 elderly with hearing loss greater than 25 dB HL and over 100,000 elderly people with disabling hearing loss of over 40 dB HL. According to current demographic projections, the numbers are expected to double in 15 years by 2030.[1] These numbers confront the challenges currently existing in

developing countries in providing affordable and accessible hearing healthcare. Given the prevalence of hearing loss in older adults, the growing demands for quality audiological services need to be adequately managed.

When comparing hearing levels between male and female participants, we found that the 4FA of male subjects were poorer than that of female subjects in all age groups. In particular, at 4 kHz, male subjects showed significantly higher thresholds than female subjects. Diminished hearing at 4 kHz is commonly associated with noise exposure. In addition to presbycusis, it is likely that there is an occupational noise-induced hearing loss (NIHL) component in males of our study cohort. Studies have shown that noise exposure alters the way ears age, and can accelerate the rate of ageing of the cochlea.[20,21] Even after the noise exposure ceases, there can be subsequent neurodegeneration that contributes to a variety of abnormal auditory perceptions. NIHL has been found to affect males at a higher rate than females, at a 3:1 ratio in the general population.[22] This could be due to men who have traditionally participated in higher noise risk activities and held occupations that had higher noise risk. The significant difference between the male and female hearing thresholds suggests the cumulative long-term effects of excessive noise. Despite the stringent laws put in place to protect the hearing of our workers, noise-induced deafness has been the top reportable occupational health disease each year since the 1970s.[23] Besides occupational noise, the use of firearms during mandatory military service, as well as recreational activities such as listening to music from portable music players, are other sources of noise risks in our population. Recently, it was found that 1 in 6 youths in Singapore are at risk of developing noise-induced deafness due to the use of portable music players.[24] Noise-induced hearing loss is entirely preventable. More efforts can be directed to educate and protect the hearing of our population.

As the study did not include an examination of the ears before the hearing test, it is conceivable that conditions such as accumulated ear wax may have contributed to an overestimation of the severity of the hearing loss. However, this study still reflects the actual hearing loss rate of the elderly in the community, whether due to presbyacusis or other reversible conditions.

Despite the fact that hearing impairment can have significant adverse effects on the emotional and social well-being of older persons,[2,25] not all elderly subjects are willing to take up hearing aids. In our study, among subjects with a disabling hearing impairment, only 7.5% (10 out of 132 subjects) used hearing aids. It is not clear from our study whether this was due to subjects being unaware of such intervention or if this was due to an outright rejection of hearing aids. It would be important to further analyse the reason for this low usage in future studies.

Nonetheless, the hearing aid ownership percentage is far lower than that found in other studies. In Taiwan, a community-based study showed that of subjects with a clinically evident hearing impairment (≥55 dB HL), only 18.4% used hearing aids.[26] In the US, only about 10% of people with mild hearing impairment and 40% of people with moderate to severe hearing impairment used hearing aids.[27] An Australian study[28] showed that of the 33% of elderly that had hearing impairment, only 11% owned a hearing aid.

A study carried out in Singapore looked into the attitudes of the elderly towards hearing aids, and found that only 33.3% responded positively to the suggestion of hearing aid use. The reasons given by the rest who were not keen to consider using hearing aids were that hearing aids were inconvenient (34%), expensive (34%), difficult to use (10%), they did not need them since they were already old (10%), or could still cope without them (23%).[4] A study conducted in Australia[29] found that multiple factors could influence a person's willingness to take up hearing aids. These include age (in this study, older people were more likely to use hearing aids), perceived severity of hearing loss and the level of support from their significant other. The participants were more likely to consider hearing aids when they found that there were more benefits than barriers to amplification, and when they were convinced that hearing aids would not be negatively perceived by others.

The cost of hearing aids can be a major deterrent, given that many of the senior citizens are retirees. In Asian populations where the elderly are often cared for by their children, it is common for them to refuse hearing aids because they do not want to trouble their children with additional financial burden. At the time of this study, hearing aid subsidies for senior citizens were not yet available. In March 2013, the Senior Mobility Fund was reviewed and expanded to provide a 90% subsidy for hearing aids to eligible seniors. This has significantly reduced the cost of hearing aid ownership and helped improve accessibility for the financially needy elderly. However, the impact of this hearing aid subsidy has yet to be assessed.

Over the last 4 years, there is growing evidence that hearing impairment is independently associated with a 30% to 40% rate of accelerated cognitive decline.[30] Individuals with mild, moderate and severe hearing impairment have a 2-, 3- and 5-fold increased risk of dementia over a 10-year follow-up period.[3] The use of hearing devices can provide increased auditory stimulation, promote social engagement and lessen cognitive load;[31] the risk of cognitive decline and dementia could potentially be reduced through the use of hearing devices, as demonstrated by the results of observational epidemiologic studies.

Our data suggests that more can be done to educate our population on hearing loss and hearing aid use. A challenge pertaining to current primary care remains. For the general practitioner who may be confronted with an older adult patient in clinic, hearing impairment is seen as secondary in the face of more pressing clinical issues. Many doctors will only address the patient's hearing difficulty when the patient or family member is persistent in bringing it to the clinician's attention. A more proactive approach needs to adopted, given that most patients do not understand the importance of hearing, unless spurred by their doctor. While the benefits of using a hearing aid should be carefully explained so that people can have a good appreciation of its benefits, the consequences of going without it should also be explained, for instance, the social and emotional impact of hearing loss and its association with cognitive decline in the elderly. Ideally, all those with hearing impairment (regardless of their initial feelings towards a hearing aid), should have a trial run of using a hearing aid to determine if they find it useful.

The HHIE-S is a well validated instrument for hearing loss screening. Studies testing the accuracy of this screening questionnaire have found that the sensitivity ranges from 36% to 72% and the specificity ranges from 78% to 92% [32,33] depending on the population. In the Blue Mountains Hearing Study conducted in Australia, researchers did a population study of 2015 elderly living in the west of Sydney. This study aimed to validate the HHIE-S against hearing loss measured by pure-tone audiometry. They found that the questionnaire yielded a sensitivity and specificity of 80% and 76%, respectively, in detecting disabling hearing loss. The study concluded that the HHIE-S was sensitive and specific enough to provide reasonable estimates of hearing loss prevalence in older adults. Interestingly, in another study by Rosis et al[34] the HHIE-S questionnaire showed low sensitivity (23.5%) and high specificity (73.7%) when the study population consisted of subjects who attended the audiological clinic. However, when the HHIE-S was administered to patients from the Geriatrics Clinic, the sensitivity was 94.7% and specificity was 75%. The study concluded that the HHIE-S questionnaire is a screening instrument that has high sensitivity and specificity in identifying hearing loss in elderly people who seek healthcare services not related to hearing disorders. In this study, the clinical setting in which the questionnaire was administered influenced the accuracy of the screening test. Self-report measures can be accurate and cost-effective screening tools for hearing loss in place of audiometric tests.

Although the HHIE-S has been accepted internationally as a useful tool for hearing loss screening in the elderly, its use in an Asian context such as Singapore has not been well validated. The accuracy of the HHIE-S may also be affected by societal differences. In our study, the sensitivity and specificity of the HHIE-S questionnaire for hearing loss >25dB HL are 36.6% and 90.8%, respectively. When tested against its performance in screening for disabling hearing impairment >40dB HL, the HHIE-S showed a sensitivity and specificity of 48% and 69%, respectively. In contrast, the Blue Mountains Hearing Study found that the questionnaire was 80% sensitive and 78% specific in detecting 4FA >45 dB HL.

The low sensitivity suggests that HHIE-S may not be the best hearing screening questionnaire for the elderly in our population. It is possible that many elderly in our society lack insight into their hearing impairment. They belong to a generation born pre-World War II or pre-independence. With more than 80% of Singapore's elderly having below secondary education, many of them had lived through difficult economic situations and thus, developed a stoic but resilient attitude towards life, resulting in a tendency to play down their inconveniences. For example, when asked, "Does your hearing difficulty make you embarrassed when you talk to strangers?" and "Does your hearing difficulty make it frustrating to talk to others in your family?", many of the elderly subjects answered in the negative despite having 4FA >40 dB HL. Cultural differences may also limit the usefulness of this questionnaire in the local Asian population. For example, a question in the HHIE-S, "Does a hearing problem cause you to attend religious services less often than you would like?", may not be applicable to a typical family.

In fact, the study by Wu et al employed a differently designed questionnaire because the researchers felt that the HHIE-S was not appropriate for local elderly patients, many of whom lead sedentary lifestyles. Their questionnaire reported a higher sensitivity (73%) but a lower specificity (64%).[4] However, it must be noted that this study looked specifically at outpatient and inpatient elderly patients, rather than in a community setting. It is interesting however, when the HHIE-S was analysed to predict hearing aid usage amongst those with disabling hearing impairment, the HHIE-S showed a 80% sensitivity and 97% NPV (Table 7). This seems to suggest that an individual's perception of his/her own hearing difficulty is a good indicator of eventual hearing aid use and benefit. It is clear that further work needs to be done in designing a questionnaire that may be reliably employed as a screening instrument for hearing impairment in Singapore's elderly population.

Conclusion

This study provides estimates on the prevalence and severity of hearing loss in older persons in Singapore. The numbers reinforce the need to develop affordable and

accessible approaches toward hearing healthcare. General practitioners and other healthcare providers can play an important role in educating the elderly and their families on the benefits of hearing aids. The HHIE-S demonstrates high specificity but low sensitivity for hearing impairment in our local community and further studies have to be done to identify a reliable screening instrument for hearing impairment in our local aged population.

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Drug Eluting Stents in Infrapopliteal Arterial Disease: A Pilot Safety Study in an Asian Population

Dear Editor,

Critical limb ischaemia (CLI) is the most severe and advanced form of peripheral arterial disease with high risk of limb loss. Almost one-third of patients undergo major amputation and one-fourth die within the first year of diagnosis.[1] Surgical re-vascularisation can reduce the number of amputations, but is often not feasible, due to the lack of suitable target and conduit vessels and comorbidities.[2]

Currently, percutaneous transluminal balloon angioplasty (PTA) is the preferred option for revascularisation of the below the knee (BTK) arterial lesions. PTA has a high technical success rate (88% to 89%),[3,4] but the long-term results are disappointing with re-stenosis rates reported to be as high as 69% at 3 months.[5]

Randomised controlled studies, as well as meta-analyses, have shown superior patency rates and clinical outcomes of drug eluting stents (DES) compared to PTA and bare metal stents (BMS), in the BTK arteries in the Western population.[6-9] However, there is no published data on the safety of DES in BTK arteries in an Asian population. This pilot study was conducted to address the safety issues and assess the short-term outcomes of this technique.

Materials and Methods

Study Design

The study was an investigator-initiated prospective single arm open-label trial. Institutional review board approval was obtained and all recruited patients gave written informed consent to participate in the study. Patients suffering from CLI (Rutherford 4,5,6) with a single arterial lesion with a length of ≤5 cm or 2 lesions with a length of ≤3 cm each within a BTK (anterior tibial, posterior tibial or peroneal) artery with expected unobstructed runoff to ankle level after treatment were eligible for the study. Iliac disease was excluded on prior Doppler ultrasound. The shorter lesion length chosen for the study was limited by the currently commercially available DES stents.[6] The entire list of inclusion and exclusion criteria is listed in Table 1.

Interventional Technique

Ipsilateral antegrade femoral access was used in all the patients, and arteriograms were performed from the common femoral artery to the pedal arch. Any femoropopliteal lesion was treated with angioplasty at the same sitting. The target lesion was imaged in 2 orthogonal planes. A total of 2000 IU of heparin was administered intra-arterially during the procedure. After successful crossing, appropriately sized DES was deployed after predilatation with a conventional balloon. We used the XIENCE V PRIME™ (Abbott, USA) stents in this study, whose safety and efficacy had been established in the Western population.[6] The procedure was defined as technically successful if the length of the target lesion was covered by the DES with a residual stenosis <20%.

Follow-up

Immediately post-procedure, the patients were commenced on clopidogrel 75 mg daily for at least 6 months and aspirin 100 mg daily for 12 months. The patients were evaluated prior to hospital discharge, and at 1, 3 and 6 months post-procedure. Earlier assessment was performed, if clinically warranted. Clinical follow-up included assessment of the Rutherford score and the ischaemic skin/ulcer changes. Duplex imaging and angiography of the treated limb was performed at the time of discharge and at 6 months post-intervention.

Endpoints

Primary endpoints for the study were primary patency of the treated lesions at 6 months after intervention on angiography. The secondary endpoints were limb salvage rate at 6 month and peri-procedural complications.

Definitions

Primary patency was defined as <50% stenosis within the stented lesion on angiography, without re-intervention in the interim. Limb salvage was defined as freedom from any major amputation at or above the ankle of the treated limb. Minor amputation was defined as amputation below the level of the ankle joint. Acute in-stent thrombosis was defined as occlusion of the stent occurring within 30 days of the intervention, late in-stent thrombosis as one which occurred anytime later than 30 days post-intervention.

Table 1. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Written informed consent	• Acute limb ischaemia
• If female patient with child-bearing potential, patient may not be pregnant at the study entry and must utilise reliable birth control for the duration of her participation into the study	• Subacute limb ischaemia which requires thrombolysis as initial treatment
• Patient is willing and able to comply with the specified follow-up evaluation	• Previous major amputation of the affected limb (at or above the level of the ankle)
• Critical limb ischaemia, this is Fontaine stage III (ischaemic rest pain) and IV (ischaemic ulcers or gangrene) or Rutherford category 4 (ischaemic rest pain), 5 (minor tissue loss) or 6 (major tissue loss)	• Concurrent iliac or femoropopliteal artery disease not suitable for endovascular or surgical revascularisation
• Stenosis (>50% luminal loss) or occlusion of infragenicular arteries (defined as: distal to the level of the popliteal artery), including the tibiofibular trunk, the anterior tibial artery, the posterior tibial artery and the peroneal artery	• Patients without (expected) distal runoff to the index site
• Infragenicular arterial lesions with a total length of ≤5 cm or 2 infragenicular lesions with a total length of ≤3 cm	• Revascularisation involving the same site within 30 days prior to the index procedure or planned revascularisation of the same limb within 30 days of the index procedure
• At least 1 crural (anterior tibial, posterior tibial or peroneal) artery with expected unobstructed runoff to ankle level after treatment	• Previous implanted stent at the index site
	• Life expectancy of less than 6 months
	• Factors making clinical follow-up very difficult or impossible
	• Known allergy to acetylsalicylic acid (aspirin), clopidogrel, heparin or paclitaxel
	• Known allergy to contrast media
	• Known heparin-induced thrombocytopaenia (HIT type 2)
	• Patient unable or unwilling to tolerate anticoagulant, antiplatelet therapy or contrast media
	• Creatinine clearance <30 mL/min (as derived from the MDRD formula) unless patient is on dialysis
	• PT/PTT of >1.5 times the median of normal that can not be corrected for the time of the procedure
	• INR >1.6 that cannot be corrected for the time of the procedure
	• Thrombocytopaenia of <50,000 which cannot be corrected for the time of the procedure

INR: International Normalised Ratio; MDRD: Modification of Diet in Renal Disease; PT: Prothrombin time; PTT: Partial thromboplastin time

Results

Study Group Demographics

Between July 2012 and December 2013,[10] CLI patients were enrolled into the study. The demographics of the study population and the comorbidities are summarised in Table 2.

Lesion and Procedural Characteristics

The lesion characteristics and the procedural details are listed in Table 3. The mean lesion length was 23.5 mm (range, 15mm to 45 mm) and the majority of the patients had severe stenosis (mean severity of stenosis: 81%, range, 52% to 99%). Nine of the patients had 1 stent deployed. One patient had 2 stents placed due to a lesion length of 45 mm. The technical success rate was 100%.

Table 2. Patient Demographics

	Patient Characteristics
Age	66 +/- 8 years
Male	8 (80%)
Right leg	6/10
Type 2 diabetes	10/10 (100%)
End-stage renal failure	5/10 (50%)
Hypertension	10/10 (100%)
Hyperlipidaemia	8/10 (80%)
Coronary artery disease	5/10 (50%)
History of smoking	5/10 (50%)
Ex-smokers	4
Current	1
Rutherford class	
4	0
5	10
6	0

Table 3. Procedural Characteristics and Follow-up

Patient ID	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Lesion Location	Distal Left ATA	Proximal Right ATA	Proximal Right ATA	Proximal Right ATA	Proximal Left ATA	Proximal Left ATA	Distal Right ATA	Distal Right ATA	Proximal Right PTA	Proximal Right ATA
Lesion severity (mean: 81%)	74%	99%	80%	80%	80%	52%	90%	61%	95%	100%
Lesion length (mean: 23.5 mm)	22	15	28	25	15	18	22	25	20	45
Stent length (mean: 35.3 mm)	28	38	38	38	28	28	28	33	28	28, 38
Stent diameter (mean: 3 mm)	3	3	3	2.5	3	3.5	3	3	3	3, 3
Balloon diameter (mm)	3	3	3	2.5	3	3.5	3	3	3	3
Rutherford score (0-5)										
At-discharge	5	Pt expired	5	5	5	5	5	5	5	5
1 month	5	Pt expired	Missed follow-up	5	5	5	5	5	5	Withdrew
3 months	4	Pt expired	1	5	5	5	4	5	5	Withdrew
6 months	0	Pt expired	Withdrew	4	5	5	5	4	0	Withdrew
Ulcer/gangrene (0 = no, 1 = yes)										
At-discharge	1	Pt expired	1	1	1	1	1	1	1	1
1 month	1	Pt expired	NA	1	1	1	0	1	1	Missed follow-up
3 months	0	Pt expired	0	1	1	1	0	1	1	Withdrew
6 months	0	NA	Withdrew	0	1	1	1	0	0	Withdrew

ATA: Anterior Tibial Artery; NA: Not Applicable; Pt: Patient

Angiographic and Clinical Endpoints

One patient died due to an unrelated cause (cardiac failure) within the first month of the study and 2 patients withdrew from the study at 1 and 6 months, respectively.

Five out of 7 patients (71%) maintained primary patency at the 6-month follow-up period. One patient presented with increased rest pain at 5 months post-enrolment. Angiogram demonstrated a severe (90%) in-stent stenosis, which was successfully treated with conventional PTA. Another patient, who was asymptomatic, had 60% in-stent stenosis noted at the scheduled 6-month follow-up angiogram, and this was treated with standard PTA.

None of the patients (7/7) underwent a major amputation until the end of the study period (6 months) as well as up to 24 months follow-up, giving a 100% limb salvage rate. Three patients underwent minor amputations (digits or forefoot) during the 24-month follow-up.

Clinical Follow-up

Of the 7 patients who completed 6 months of clinical follow-up, none showed worsening of their Rutherford score or development of new skin ischaemia during the study period. Four of the 7 patients had complete resolution of the minor tissue loss, which were present at the time of recruitment into the study. The mean baseline improvement in Rutherford score was 1.7 (range, 0-5). The clinical follow-up details are summarised in Table 3.

Complications

There were no peri-procedural access site complications. There was no incidence of acute or late in-stent thrombosis. One patient developed upper gastro-intestinal bleeding (UGIB) due to the dual antiplatelet therapy (DAPT) which settled spontaneously after withdrawal of the medications.

Discussion

Peripheral arterial disease in the Asian population involves the supra- and infra-popliteal arterial segments with diffuse heavily calcified non-occlusive pattern of disease. This is mainly due to the high prevalence of diabetes and renal failure in this group of patients which causes small vessel disease.[10,11] This is reflected in our cohort (100% were diabetic and 50% had end-stage renal failure). Singapore has a high prevalence of diabetes (11%) which is increasing.[12] A recent meta-analysis has shown that DES has significantly better long-term outcomes in diabetic patients with amputation-free survival rates of 94.1% and 90.4%, at 1 and 5 years, respectively.[13] Hence, DES may prove to be a useful treatment in our patient population to improve their clinical outcomes.

In our study, all patients presented with advanced CLI (Rutherford 5) compared to those included in the previous studies (50% to 68%).[6,7] However, our primary patency rates (71% at 6 months) are comparable to those reported in earlier trials in the Western population (86% at 6 months).[7] DES appears to be relatively safe in our small study population with no incidence of acute/late in-stent thrombosis during the follow-up period.

The limitations of our study are that it was a single arm non-randomised study design, with a small sample size and potential for selection bias. The study was limited to the evaluation of short focal lesions due to constraints of short stent lengths and the number of stents that could be used in each patient. As the evidence grows stronger in favour of DES, longer stents may become available in the future, to address the longer lesions seen in real life practice.

Conclusion

The findings of our study suggest that DES can be safely used in the treatment of BTK arterial disease in Asian CLI patients. Further large studies are required to confirm the safety and efficacy of DES in this group of patients.

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A Case Report of Clear Cell Papulosis and a Review of the Literature

Dear Editor,

Clear cell papulosis (CCP) is a rare dermatosis seen predominantly in infants of Asian background. It presents with hypopigmented and minimally palpable, flat-topped papules, sited over the lower abdominal or pubic regions, or along the milk lines.

We present a series of 3 local patients with CCP, highlighting their clinicopathologic characteristics and review the existing literature of published cases. Two cases of this series have been previously published.[1,2]

Case 1

A healthy 16-month-old Chinese female presented in 2003 with 2 hypopigmented macules and 1 flat-topped papule in the pubic region, ranging from 3 mm to 9 mm in diameter. These were not preceded by trauma or inflammation. The lesions were asymptomatic. The rest of her skin examination was normal. There was no family history of similar lesions.

Histopathologic examination showed proliferation of clear cells, with round to oval nuclei and abundant cytoplasm, arranged either in clusters or singly along the basal and suprabasal epidermis. There was also mild epidermal acanthosis, and reduced melanin pigmentation.

The cytoplasm of these cells stained positively with mucicarmine, periodic-acid Schiff (PAS) and alcian blue. Immunohistochemical profile of these cells was: +CEA, +EMA, +AE1/3, +CK7, +CAM5.2, –GCDFP, –CK20, –S100.

At 1-year follow-up, the patient's lesions remained unchanged.

Case 2

An 18-month-old Chinese male presented in 2005 with multiple asymptomatic, slightly elevated and hypopigmented papules for 3 months. These were seen at the lateral aspects of his lower abdomen and groin. There were also lesions on an area adjacent to the right nipple. Individual lesions were 1 mm to 3 mm in size. There was no family history of similar lesions.

Histopathologic findings were consistent with clear cell papulosis, showing round to oval clear cells with abundant clear cytoplasm located in clusters or singly amongst basal keratinocytes. These cells were larger than adjacent keratinocytes and stained positively with PAS. Immunohistochemistry was positive for CEA and AE1, but negative for S100.

The patient defaulted on follow-up.

Case 3

A 3-year-old Chinese male presented in 2015 with asymptomatic, hypopigmented macules since 7 months' age. They first appeared on his penile shaft and progressively spread to the suprapubis (Fig. 1), abdomen and axilla. There was no family history of similar lesions.

Histopathologic findings confirmed CCP, with increased numbers of large clear cells in the basal epidermis. These cells had larger, more vesicular nuclei and abundant clear cytoplasm (Fig. 2) which stained positively for PAS. Staining with CK7 was positive, highlighting similar cells in the suprabasal epidermis and "tadpole-tail" like projections of some cells (Fig. 3).

The lesions remained unchanged over a 3-month period of follow-up and the patient will continue to be seen annually.

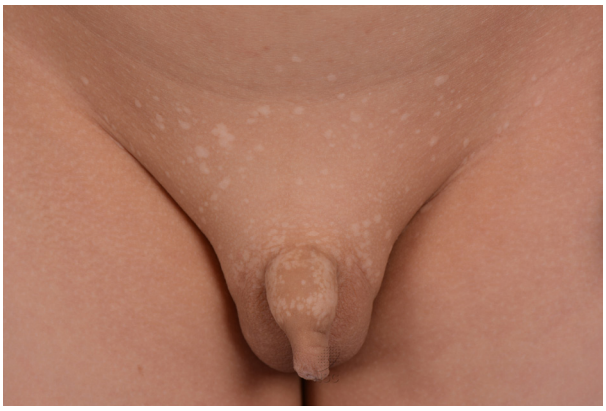

Fig. 1. Hypopigmented macules and barely palpable papules over the penile shaft and suprapubis.

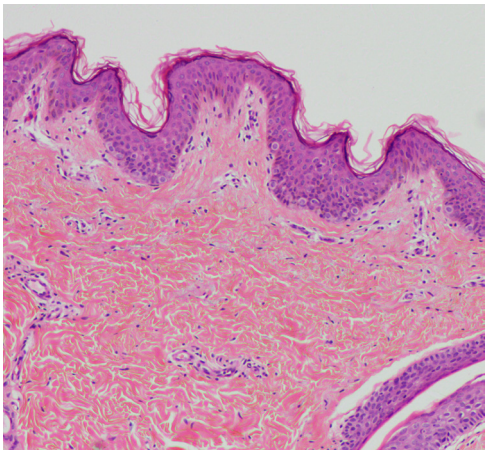

Fig. 2. Proliferation of clear cells in the basal epidermis, larger than adjacent keratinocytes (H&E, 100x).

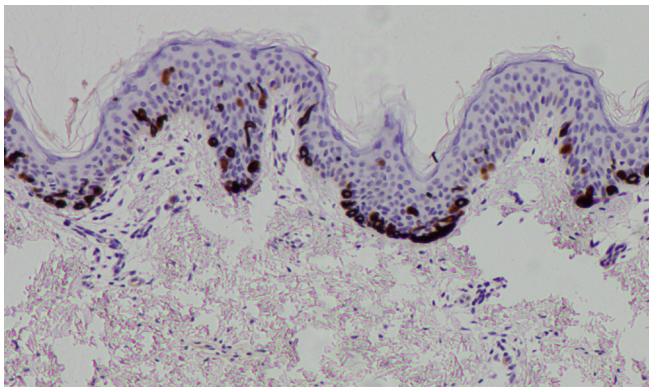

Fig. 3. Positive staining with CK7. Scattered clear cells in the suprabasal epidermis are more evidently seen. A "tadpole tail"-like projection is present in some cells (100x).

Discussion

Kuo et al first described CCP in 2 Taiwanese brothers in 1987.[3] To date, only 35 cases have been reported in the literature. We describe our 3 local cases (2 were previously published) and compare their clinical and histopathologic features (Table 1).

All 3 cases presented with typical hypopigmented, barely palpable papules and macules in the characteristic anatomical distribution of the pubic, inguinal or lower abdominal regions. The lesions were asymptomatic and non-progressive. Demographically, all patients were of Chinese ethnicity and the onset was in infancy. Family history was non-contributory in all cases. Histopathologic features were consistent in all 3 cases, showing characteristic larger cells with abundant clear cytoplasm in the basal epidermis. These clear cells stained positively for mucin, as well as CK7, CEA and AE1/3. S100 immunohistochemistry was negative in all cases.

Our 3 cases are similar to other reports (Table 2) in terms of clinical, demographic and histopathologic features. Individual lesions are small and there have been no reports of lesions greater than 1 cm; the number of lesions can vary from 3 to over 100. Lesions have a predilection for the abdomen, particularly the lower half (81%, 29/36 cases) and the pubic area (56%, 20/36 cases). Other common sites include the chest (42%, 15/36 cases) and axilla (33%, 12/36 cases). Lesions have been observed to follow the milk line.[4] The back, buttocks and extremities are seldom involved.[5,6]

Epidemiologically, only 6 out of 36 cases were of non-Asian ethnicity. The overall mean age of onset is 13.9 months (range, 0 to 71 months); however, 1 case of CCP occurring in adulthood has been reported.[7] Although some authors have postulated a possible autosomal recessive mode of inheritance,[5] contributory family history is only observed in a quarter of patients (9/36 cases).

The distinctive clinical characteristics of CCP enable it to be distinguished from other paediatric hypopigmented dermatoses. Differential diagnoses with potential therapeutic or prognostic differences include plane warts, tinea versicolor-like lesions of epidermodysplasia verruciformis, guttate morphoea and lichen sclerosus.

Histopathological findings can readily differentiate between CCP and the aforementioned clinical differentials based on the histologic hallmark of a proliferation of larger clear cells within the basal epidermis. These cells exist singly or in small clusters, and can be found within the spinous or granular layers, albeit in smaller numbers.[3] They are larger than adjacent keratinocytes and do not show cellular atypia.[5] Majority of these cells show positive staining for mucin (82.6%, 19/23 cases). A cytoplasmic “tadpole-tail”-like process that is directed superficially has been described.[3] Other minor co-existing features include mild acanthosis, mild hyperkeratosis and decreased basal melanin.

Multiple immunohistochemical stains have been used to detect the cells of CCP. [3-14] The most commonly used stains include AE 1/3 (21/21 cases positive), CEA (21/21) and EMA (18/18). Negative staining with S100 (17/17) is also consistently observed. Other less commonly used stains include CK7 (8/8), GCDFP (6/7) and CAM5.2 (5/5).

Pathogenetically, Toker cells have been postulated to be the cell of origin in CCP, given their similar anatomical distribution (“milk line” configuration) and histological features. They also share similar immunohistochemical profiles, with both staining positively for EMA, CK7 and other low-molecular-weight cytokeratins.[15] However, Toker cells differ as they stain negatively for polyclonal

Table 1. Characteristics of the 3 Singaporean Cases of CCP

	Age at Presentation (Months)	Race	Sex	Age of Onset (months)	Site of Involvement	No. of Lesions	Diameter of Lesions	FHX	Mucin Staining	Positive IHC	Negative IHC
Case 1*	16	Chinese	F	NR	Pubic	3	3 mm to 9 mm	Nil	Positive for mucicarmine, alcian blue, PAS	AE1/3 CEA EMA CAM5.2 CK7	S100 CK20 GCDFP
Case 2†	18	Chinese	M	15	Groin, lower abdomen, chest	Multiple	1 mm to 3 mm	NR	Positive for PAS	AE1 CEA	S100
Case 3	36	Chinese	M	7	Pubic, genitals, abdomen axilla	Multiple	NR	Nil	Positive for PAS	CK7	

CAM5.2: Cell adhesion molecule 5.2; CEA: Carcinoembryonic antigen; CK7: Cytokeratin-7; CK20: Cytokeratin-20; EMA: Epithelial membrane antigen; F: Female; FHX: Family history; GCDFP: Gross cystic fluid disease protein; IHC: Immunohistochemistry; M: Male; NR: Not reported; PAS: Periodic acid-Schiff

*Kumarasinghe SP, Chin GY, Kumarasinghe MP. Clear cell papulosis of the skin: a case report from Singapore. Arch Pathol Lab Med 2004;128:e149-52.

†Chong WS, Ong BH, Kumarasinghe SP. Hypopigmented papules in an Asian boy. Pediatr Dermatol 2005;22:268-9.

Table 2. Summary of 33 CCP Cases Reported in the Worldwide Literature

Author	No. of Cases/ Ethnicity	Sex	Onset Age (Months)	Site	Lesion Count	Other Histologic Features	Mucin	Positive IHC Stains (Negative Stains in Parenthesis)	Follow-up	FHX
Kuo*, 1987	2/Taiwanese	M	Birth	Shoulders, chest, abdomen, pubic	15	• Moderate hyperkeratosis • Moderate acanthosis • Decreased basal pigmentation • Slight disorganisation of keratinocytes	+	AE1/AE3 CEA EMA (S100)	NR	Patients were brothers
		M	7	Chest, abdomen	5					
Kuo†, 1995	3/Taiwanese	M	12	Lower abdomen	5	• Mild hyperkeratosis • Moderate acanthosis • Decreased basal pigmentation • Slight disorganisation of keratinocytes	+	AE1 CEA EMA GCDFP	NR	Nil
		M	24	Lower abdomen, inguinal area	>100					
		F	NR	Lower abdomen, chest	20					
Kim‡, 1997	1/Korean	F	10	Lumbar area, buttocks	Numerous	• Mild hyperkeratosis • Mild acanthosis • Decreased basal pigmentation	+	AE1 CEA EMA IKH4 CAM5.2 (S100)	NR	Nil
Lee§, 1998	4/Taiwanese	F	24	Axilla, chest, abdomen, pubic, groin	100	• Mild acanthosis • Decreased melanisation of epidermis, but normal number of basal melanocytes	+	AE1/AE3 CEA EMA (S100)	NR	First 2 patients are sisters
		F	20	Pubic	Few					

CAM5.2: Cell adhesion molecule 5.2; CEA: Carcinoembryonic antigen; CK7: Cytokeratin-7; CK20: Cytokeratin-20; EMA: Epithelial membrane antigen; ER: Estrogen receptor; FHX: Family history; GCDFP: Gross cystic fluid disease protein; Her2: Human epidermal growth factor receptor-2; IHC: Immunohistochemistry; NR: Not reported; PR: Progesterone receptor

*Kuo TT, Chan HL, Hsueh S. Clear cell papulosis of the skin. A new entity with histogenetic implications for cutaneous Paget's disease. Am J Surg Pathol 1987;11:827-34.

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§Lee JY, Chao SC. Clear cell papulosis of the skin. Br J Dermatol 1998;138:678-83.

‖Gianotti R, Cambiaghi S, Locatelli A, Gelmetti C. Clear cell papulosis (pagetoid papulosis) in a non-Asian patient. Dermatology 2001;203:260-1.

¶Mohanty SK, Arora R, Kakkar N, Kumar B. Clear cell papulosis of the skin. Ann Diagn Pathol 2002;6:385-8.

#Benouni S, Kos L, Ruggeri SY, North PE, Drolet BA. Clear cell papulosis in Hispanic siblings. Arch Dermatol 2007;143:358-60.

**Farley-Loftus R, Bossenbroek NM, Rosenman K, Schaffer JV. Clear cell papulosis. Dermatol Online J 2008;14:19.

††Yu Y, Sukhatme S, Loo DS. Clear cell papulosis: a connection of clear cells to toker cells or paget disease. Arch Dermatol 2009;145:1066-8.

‡‡Tseng FW, Kuo TT, Lu PH, Chan HL, Chan MJ, Hui RC. Long-term follow-up study of clear cell papulosis. J Am Acad Dermatol 2009;63:266-73.

§§Sim JH, Do JE, Kim YC. Clear cell papulosis of the skin: acquired hypomelanosis. Arch Dermatol 2011;147:128-9.

‖‖Wysong A, Sundram U, Benjamin L. Clear-cell papulosis: a rare entity that may be misconstrued pathologically as normal skin. Pediatr Dermatol 2012;29:195-8.

Table 2. Summary of 33 CCP Cases Reported in the Worldwide Literature (Cont'd)

Author	No. of Cases/ Ethnicity	Sex	Onset Age (Months)	Site	Lesion Count	Other Histologic Features	Mucin	Positive IHC Stains (Negative Stains in Parenthesis)	Follow-up	FHX
		M	21	Lower abdomen, pubic	Few					
		F	4	Axilla, chest, abdomen, pubic	Numerous					
Gianotti‖, 2001	1/Italian	F	6	Chest, lower abdomen, pubic	NR	• Mild acanthosis	NR	AE1 CEA EMA (S100)	NR	NR
Mohanty¶, 2002	1/Indian	F	44 years	Chest, lumbar area, abdomen	6	• Mild hyperkeratosis • Mild acanthosis • Decreased basal pigmentation	–	AE1/3 CEA EMA (S100)	Nil progression over 5 months	Nil
Benouni# 2007	3/Hispanic	M	8	Lower abdomen, pubic, axilla	50	• Decreased melanisation of lesional epidermis	–	CEA CK7 HMW cytokeratin (S100, CD1a)	NR	First 2 patients are siblings
		F	71	Chest, abdomen, pubic	NR					
		M	23	Axilla, abdomen, pubic, groin	NR	• Nil	+	CEA CK7 EMA (S100, CD1a)		

CAM5.2: Cell adhesion molecule 5.2; CEA: Carcinoembryonic antigen; CK7: Cytokeratin-7; CK20: Cytokeratin-20; EMA: Epithelial membrane antigen; ER: Estrogen receptor; FHX: Family history; GCDFP: Gross cystic fluid disease protein; Her2: Human epidermal growth factor receptor-2; IHC: Immunohistochemistry; NR: Not reported; PR: Progesterone receptor

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Table 2. Summary of 33 CCP Cases Reported in the Worldwide Literature (Cont'd)

Author	No. of Cases/ Ethnicity	Sex	Onset Age (Months)	Site	Lesion Count	Other Histologic Features	Mucin	Positive IHC Stains (Negative Stains in Parenthesis)	Follow-up	FHX
Farley-Loftus[**], 2008	1/Chinese	M	3	Abdomen, pubic	>50	• Mild acanthosis & papillomatosis	+	NR	NR	Nil
Yu[††], 2009	1/Asian-American	F	8	Axilla, chest, pubic, genitalia, buttocks	Numerous	• Mild acanthosis	+	CK7 CAM5.2 CEA AE1/3 EMA GCDFP (S100, Her2, ER, PR, p53)	NR	NR
Tseng[‡‡], 2009	14/Taiwanese	10F 4M	12 (median)	Abdomen, pubic area, chest, axilla, groin, extremities	2 – >100	• Mild hyperkeratosis • Mild to moderate acanthosis • Decreased basal pigmentation	3/3 +	AE1 (5/5) CEA (2/2) EMA (2/2) GCDFP (1/1) CAM5.2 (1/1)	Reduction in lesion count (10/11) Increase in lesion size (1/11)	3 patients with affected siblings
Sim[§§], 2011	1/Korean	F	2	Chest, abdomen, pubic	NR	• Mild hyperkeratosis • Mild acanthosis • Decreased melanisation of epidermis, but normal number of basal melanocytes	NR	CK7 EMA CEA (S100, CD1a)	NR	Nil
Wysong[‖‖], 2012	1/Indian	F	9	Axilla, chest, pubic	NR	• Nil	–	AE1 CK7 CAM5.2 GCDFP (S100, ER, PR)	NR	NR

CAM5.2: Cell adhesion molecule 5.2; CEA: Carcinoembryonic antigen; CK7: Cytokeratin-7; CK20: Cytokeratin-20; EMA: Epithelial membrane antigen; ER: Estrogen receptor; FHX: Family history; GCDFP: Gross cystic fluid disease protein; Her2: Human epidermal growth factor receptor-2; IHC: Immunohistochemistry; NR: Not reported; PR: Progesterone receptor

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CEA and mucin.[8,15] Of importance, Toker cells have been implicated as the precursors of Paget's disease. However, Tseng et al demonstrated that none progressed to Paget's disease in their cohort of 19 CCP patients. These patients were followed-up over a median of 11.5 years;[5] 64.3% showed a reduction in lesion count while 21.4% showed complete resolution.[5]

Conclusion

CCP is a rare but distinctive infantile dermatosis with characteristic clinical and histologic findings. Lesions are asymptomatic and longitudinal follow-up of cases has demonstrated a benign course. Hence, no treatment is necessary.[5] More research is needed to elucidate the exact cell of origin.

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Acquired Platelet Dysfunction with Eosinophilia or Idiopathic Purpura with Grey Platelets?

Dear Editor,

An acquired, transient bleeding disorder characterised by a thrombocytopathic bleeding with a platelet storage pool disorder has been reported from the Southeast Asian region and elsewhere since the 1960s.[1,2] The condition has been coined acquired platelet dysfunction with eosinophilia (APDE) as cases reported earlier were also found to have eosinophilia. However, a large series of cases published in the 21st century shows that 14% of the affected children do not have eosinophilia.[3] The following cases also illustrate that significant eosinophilia is not a constant feature (Table 1). Idiopathic purpura with grey platelets is proposed as a better terminology to describe the condition, so long as the aetiology remains obscure.

Case 1 is a Eurasian 5-year-old male who presented with abrupt onset of generalised ecchymosis and scattered petechiae. Non-accidental injury was initially suspected and hence, he was brought to medical attention. Multiple bruises and petechiae were found in the extremities and a couple of ecchymosis were seen on the trunk. The child was otherwise well and no other abnormal signs were seen. The complete blood count was normal with mild eosinophilia (0.75×10^9/L). The peripheral blood film revealed plenty of grey platelets and the results of platelet aggregation were consistent with a platelet storage pool disorder. His bleeding symptoms resolved without treatment after 2 months.

Case 2 is a 4-year-old Chinese female who presented with recent onset of generalised bruises and petechiae. The complete blood count was marked by extreme eosinophilia (4.81×10^9/L). On the peripheral blood film, grey platelets with eosinophils were abundant (Fig. 1A). Platelet aggregation abnormalities were consistent with a storage pool defect. Her bleeding symptoms resolved a month later. A repeat test 8 months later while she was evaluated for skin allergy showed platelet and eosinophil counts of 377 and 1.09×10^9/L, respectively, with disappearance of the grey platelet on the blood film.

Case 3 is a 3-year-old female of Indian descent who presented with an abrupt onset of generalised bruises mainly on the lower limb and abdominal wall. The complete blood count was normal and no eosinophilia was found. However, grey platelets were seen under the microscope (Fig. 1B)

Table 1. Summary of Haematologic Findings in the 3 Cases

	Case 1	Case 2	Case 3	Normal Ranges
Sex/age, year	Male/5.3	Female/4.7	Female/3.7	-
Hb, g/dL	13.0	13.0	11.1	-
WBC, $\times 10^9$/L	6.80	13.35	9.74	-
Eosinophil, $\times 10^9$/L	0.75	4.81	0.29	-
Platelet, $\times 10^9$/L	153	269	173	-
Platelet aggregation tests with:				
ADP	44%	61%	50%	64% to 111%
Collagen	13%	9%	25%	68% to 117%
Epinephrine	12%	25%	23%	46% to 122%
Ristocetin	100%	82%	87%	80% to 115%
Arachidonic	82%	74%	78%	52% to 110%

ADP: Adenosine diphosphate; Hb: Haemoglobin; WBC: White blood cells

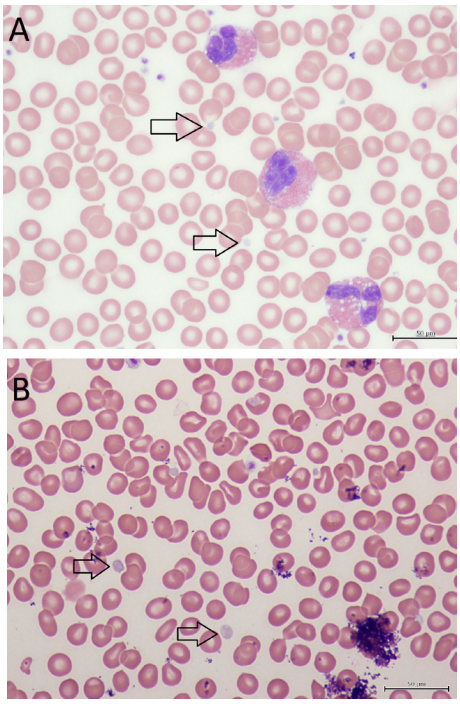

Fig. 1. Photomicrographs from Cases 2 and 3, A) and B) respectively, showing at least 50% of the platelets on the peripheral blood film are devoid of normal contents and thus appear as grey platelets. Eosinophilia is obvious in Case 2 but absent in Case 3.

and a platelet storage pool disorder was evident on platelet aggregation tests. She recovered without treatment a month later with the disappearance of the grey platelets on blood film.

Idiopathic thrombocytopaenic purpura (ITP) is the most common cause of acquired bleeding disorder in childhood. The name clearly defines the cardinal clinical and laboratory features and the diagnosis is usually straightforward. APDE, in contrast, does not fulfill the same purpose. Platelet dysfunction has to be defined by specific platelet aggregation tests, which is only available in specialised laboratories and the results may take a few days to turn around. While extreme eosinophilia was common in earlier reports like Case 2, a recent series of 168 children reported from Thailand shows a wide range of eosinophil counts and 14% do not have eosinophilia at all.[2] In this respect, eosinophilia may be an epiphenomenon seen in communities with endemic parasitic infections and allergic disorders. Thus, APDE is an inconvenient and inaccurate name to describe the condition and may distract the unfamiliar clinician from making the diagnosis. Indeed, as illustrated by Case 2, eosinophilia may persist even when the thrombocytopathic bleeding diathesis has resolved.

Hence, idiopathic purpura with grey platelets may be a better terminology. Cutaneous bruises with or without petechiae, clinically indistinguishable from ITP, are universally present. The condition can be rapidly recognised when grey platelets are found under the microscope in the absence of thrombocytopaenia. Thus, a presumed diagnosis can be made in any laboratory providing routine haematology service. Additional tests on platelet dysfunction to document a storage pool disorder will lend support to the diagnosis.

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Dr Robert Loh Choo Kiat, *JP, BBM, PJG* (1925 – 2017)*

Dr Robert Loh Choo Kiat was born in Singapore in 1925. His education was interrupted by World War II, but he graduated with MBBS in 1949 from Bombay's top medical school, the Seth Gordhandas Sundahas Medical College and the King Edward VII Memorial Hospital. He returned to Singapore soon after, joining the Singapore General Hospital (SGH).

Thankfully for us, ophthalmology was to be his passion and his career-long discipline. He subsequently underwent postgraduate training under top ophthalmologists including Sir Stewart Duke-Elder (known as the "Father of Ophthalmology") at the world-renowned Moorfields Hospital in London, before he returned to SGH, joining the Eye Department at Norris Block, as a Registrar in 1954.

In 1958, Dr Loh was awarded a scholarship to take the FRCS Edinburgh examination (which he passed), returning soon after as a young Head of the Department of Ophthalmology. Dr Wong Kin Yip and Dr Loh were the first Singaporean Heads of Ophthalmology in the public sector. They started the long and tortuous journey, teaching and building up the clinical service, and reputation of SGH's ophthalmology department.

Dr Loh's contributions to the field of Ophthalmology in Singapore have been immense. From a small department of only a handful of ophthalmology trainees, he built up and trained numerous expert eye surgeons within a decade and instituted in them his ideals and values in the treatment of patients, regardless of their social status.

Among these contributions included the establishment of the first Eye Bank, introduction of micro and laser surgery, lens implants, retinal detachment surgery, corneal grafting and other innovative procedures that we take for granted today.

Early in the 1960s, Dr Loh set up the Singapore Society of Ophthalmology (SSO) with only 13 members and was

Third APAO Congress held in 1968 with Congress President, Dr Robert Loh (seated in front row, 12th from the right).
Photo courtesy of the family of Dr Robert Loh.

*A similar tribute article on Dr Robert Loh by Prof Chew Chin Hin has been published in an Eulogy in SMA News, Vol. 49, No. 4, April 2017 issue.

Dr Robert Loh (seated in front row, 5th from the right) at the AMS' Annual Induction Comitia Dinner held on 16 April 1970.

elected as its founding President for more than a decade (1963-1976). Today, SSO has a membership of more than 200 ophthalmologists. The Society laid the foundation for the formation of the Chapter of Ophthalmologists, which subsequently transformed to become the College of Ophthalmologists of the Academy of Medicine, Singapore (AMS). In 1964, Dr Loh was elected as President, Singapore Medical Association (SMA), being one of only 2 ophthalmologists who has served as the President of the SMA.

In 1968, Dr Loh hosted the 3rd Asia Pacific Academy of Ophthalmology (APAO) meeting successfully in Singapore. As Congress President of this relatively new meeting, he laid the foundation that allowed the College of Ophthalmologists and SSO to bid and successfully bring the APAO Congress back to Singapore. In March 2017, Singapore hosted the 32nd APAO Congress, with more than 5200 delegates from over 75 countries.

During the 1960s, Dr Loh also served on the AMS Council, advancing much of Singapore's postgraduate specialty training programmes and higher examinations. In 1975, he was elected as Master of the Academy of Medicine, Singapore where he served until 1978.

Charity was also a lifetime commitment to Dr Loh, and he led the YMCA, a Christian charity from 1970, where he served wholeheartedly for over 20 years. He was conferred President Emeritus in 1993. For his dedicated commitment in service to the community, he was appointed by the Singapore Government to lead the newly restructured National Council of Social Service in 1992 as its first President. It was only in 2002 that he retired.

While many do not personally know nor have the privilege to meet or interact with Dr Loh, ophthalmology colleagues in Singapore have been one of the significant beneficiaries of Dr Loh's vision, legacy and foundation building work in the early formative years of Singapore ophthalmology in the 1950s and 1960s. Today, Singapore ophthalmology has a global, leading reputation as a centre of excellence and we are where we are only because we are reaping the fruits of the work of giants such as Dr Loh. We must and will continue to uphold his vision, dedication and legacy.

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