ANNALS
ACADEMY OF MEDICINE, SINGAPORE
COMMITTED TO SPECIALIST EDUCATION AND TRAINING SINCE 1957

DIAMOND JUBILEE CELEBRATION 1957-2017 60 years

VOLUME 47 | NUMBER 5 | FREE PAPERS | MAY 2018

MCI (P) 104/07/2017

"It is a rough road that leads to the heights of greatness."

Lucius Annaeus Seneca (4 BC – AD 65)
Roman philosopher

Reproduced with permission from:
Anonymous

Please see inside Contents for the full list of articles.

Acknowledgements

The Editorial Board of the Annals, Academy of Medicine, Singapore gratefully acknowledges the generous support of:

The Lee Foundation

*****

Forthcoming Issues

Vol 47 No. 6, June 2018 – Free Papers
Vol 47 No. 7, July 2018 – Free Papers
Vol 47 No. 8, August 2018 – Free Papers
Vol 47 No. 9, September 2018 – Free Papers
Vol 47 No. 10, October 2018 – Free Papers

* * * * *

General Information

* * * * *

For all enquiries, please contact the Annals Editorial Office at: Annals, Academy of Medicine, Singapore, 81 Kim Keat Road, #11-00 & 12-00, NKF Centre, Singapore 328836. Email: annals@ams.edu.sg; Homepage: http://www.annals.edu.sg

Online submission: http://www.annals.edu.sg/OnlineManuscript/

We welcome submissions of cover images from Fellows and Friends of the Academy of Medicine for consideration for publication. Do submit interesting or unusual photographs or digitised images of original artwork, accompanied by a short write-up of about 30 words.

Format: 8 by 12 cm, resolution of at least 300 dpi, in JPEG or TIFF. Please email your submission to annals@ams.edu.sg

Printed by Straits Printers (Pte) Ltd

ISSN 0304-4602

MCI (P) 104/07/2017

ANNALS
ACADEMY OF MEDICINE SINGAPORE

Free Papers

Editorial

Body, Heart and Mind: The Battle Against Tobacco Continues

Adeline Seow, [1] *MBBS, MMed (Public Health), FFPH (UK)*

Tobacco use continues to impact health on a global scale. In 2015, 11.5% of all deaths worldwide (or a total of 6.4 million deaths) were attributable to tobacco, and more than half (52.2%) occurred in 4 countries—China, India, the United States (US) and Russia.

This year's World No Tobacco Day focuses on the impact of tobacco use on heart disease.

Two-fifths (41.2%) of the disability-adjusted life-years lost which were attributable to smoking were due to cardiovascular diseases, followed by cancers (27.6%), and chronic respiratory diseases (20.5%).[1]

Smoking remains one of the major preventable causes (with hypertension, obesity and diabetes) of cardiovascular disease in Asian populations, especially among men. The InterHeart Study, a case-control study that enrolled 15,152 cases and 14,820 controls worldwide reported that, across different regions in Asia, smoking accounts for 39-45% of myocardial infarction among men and 7-15% among women.[2] Using data from the Asia-Pacific Cohort Studies Collaboration, Peters et al[3] showed that while hypertension was the most prominent single risk factor for cardiovascular disease among Asians, the population attributable fraction (PAF) was highest for men who were both hypertensive and smokers (PAF 37%).

The Framework Convention on Tobacco Control (FCTC)—introduced by the World Health Organization (WHO) in 2003—has been the mainstay of global efforts to combat tobacco use. The FCTC places legally binding obligations on countries to implement a series of strong and effective measures. Singapore, which ratified the treaty in 2004, is one of 180 countries that are party to the Convention. In the decade since the treaty came into force, there has been substantial progress in maintaining a decline in smoking prevalence rates.[4]

The key measures within the FCTC which focus on reducing demand, and allow countries to track their progress are: monitoring tobacco use and prevention policies, protecting people from tobacco smoke, providing cessation programmes, pack warnings, bans on advertising, promotion and sponsorship and raising cigarette taxes.[5] Based on data collected by the WHO, 63% of the world's population (about 4.7 billion people, including 59% of those living in low- and middle-income countries) are now covered by at least one measure at the "best-practice" level, up from 15% in 2007.[4]

Despite the progress made, the fact remains that implementation is most challenging (and disease burden highest) in lower- and middle-income countries, and that women and young people in these countries continue to be targeted by the tobacco industry.[6] In countries that are able to enact strong antitobacco policies in line with the FCTC (particularly increasing taxes on cigarettes), this not only substantially improves population health as a whole, but also reduces social inequalities in cardiovascular mortality within populations.[7,8]

Moving ahead, questions have been raised about how effective a "business-as-usual" approach to the FCTC will be in turning the tide; with visionaries calling for stronger measures and more coordinated efforts in order to achieve a tobacco-free world (<5% smoking prevalence) by 2040.[9] What is clear is that the social and political impetus to implement and enforce tobacco control policies in countries like China (which is home to almost one-third of all smokers worldwide) will make the largest impact on whether this vision can be realised.

Nevertheless, based on the metrics that WHO uses to track progress among countries, it is clear that there is a large variation in the extent to which each country has achieved the standards the WHO has set through its global initiatives. Among the 100 largest cities in the world, Singapore is ranked in the top category in only 2 of the 5 measures that WHO considers critical at a policy level.[10] The inter-relationships are also worth thinking more deeply about. Notably, as the list of places this city-state designates as "smoke-free" grows, the need for effective, affordable and accessible cessation services comes to the fore.

Even closer to home (particularly for readers of this journal), reducing the harms of smoking is ultimately a

[1]Saw Swee Hock School of Public Health, National University of Singapore, Singapore
Address for Correspondence: A/Prof Adeline Seow, Saw Swee Hock School of Public Health, National University of Singapore, Tahir Foundation Building, 12 Science Drive 2, #10-01, Singapore 117549.
Email: ephseowa@nus.edu.sg

battle fought at the level of an individual's body, heart and mind; and medical professionals are in a position to make a difference. One in 4 (25.4%) Singaporean males and 1 in 25 (4.8%) Singaporean females are daily smokers based on the National Health Surveillance Survey 2012.[11] In a clinical setting, the prevalence could be much higher, but previous reports suggest that not enough is done to identify and act on patients' smoking status.[12] A report by the US Public Health Service[13] noted that (with a smoking prevalence rate of 18-21%),[14] 70% of US smokers visit a clinician each year, giving clinicians and healthcare systems "unparalleled access" to smokers. Smoking cessation may be the single most effective intervention to reduce risk of death from heart disease or stroke, especially among individuals with established cardiovascular disease. Among patients with coronary artery disease, smoking cessation is estimated to lead to a 35% reduction in mortality risk.[15] The benefit of stopping smoking has been shown to accrue within 4-6 years, and extends to both young and older smokers.[16]

There is no easy route to smoking cessation. Tobacco dependence is a condition that requires ongoing assessment and repeated interventions. Treating dependence is, admittedly, a process that requires coordination across the healthcare system, and one that often falls through the cracks. Notwithstanding, using the '5As' (or the more concise '2A & R' [Ask, Advise and Refer]) approach has been shown to take as little as 3 minutes, to effectively increase the likelihood of an attempt to quit; and is a standard recommendation for clinicians.[13]

Initiating a conversation about smoking during a consultation takes effort, and research has shown that clinicians are more likely to bring this up if patients already have established smoking-related disease,[17] or if they are perceived as more proactive about their health.[18] The same studies found, however, that the positive impact of a doctor's advice on the likelihood that patients will attempt to quit is not dependent on having the disease or on the level of engagement.

Asking, offering unambiguous, non-judgemental advice, and facilitating access to counselling or therapy are interventions that have been shown to be clinically effective across different populations and should be part of care for every patient. For patients at higher risk of (or who already have) heart disease, the need is greater and the stakes higher, but the potential benefit of 'Ask, Advise and Refer' in any clinical encounter extends to all individuals, and must continue to be part of the strategy in this ongoing battle.

REFERENCES

1. GBD 2015 Tobacco Collaborators. Smoking prevalence and attributable disease burden in 195 countries and territories, 1990-2015: a systematic analysis from the Global Burden of Disease Study 2015. Lancet 2017;389:1885-906.
2. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004;364:937-52.
3. Peters SAE, Wang X, Lam TH, Kim HC, Ho S, Ninomiya T, et al. Clustering of risk factors and the risk of incident cardiovascular disease in Asian and Caucasian populations: results from the Asia Pacific Cohort Studies Collaboration. BMJ Open 2018;8:e019335.
4. WHO Report on the Global Tobacco Epidemic, 2017: Monitoring Tobacco Use and Prevention Policies. Geneva: World Health Organization; 2017.
5. WHO Report on the Global Tobacco Epidemic, 2008: The MPOWER Package. Geneva: World Health Organization; 2008.
6. Gilmore AB, Fooks G, Drope J, Bialous SA, Jackson RR. Exposing and addressing tobacco industry conduct in low-income and middle-income countries. Lancet 2015;385:1029-43.
7. Hill S, Amos A, Clifford D, Platt S. Impact of tobacco control interventions on socioeconomic inequalities in smoking: review of the evidence. Tob Control 2014;23:e89-97.
8. Allen K, Kypridemos C, Hyseni L, Gilmore AB, Diggle P, Whitehead M, et al. The effects of maximising the UK's tobacco control score on inequalities in smoking prevalence and premature coronary heart disease mortality: a modelling study. BMC Public Health 2016;16:292.
9. Beaglehole R, Bonita R, Yach D, Mackay J, Reddy KS. A tobacco-free world: a call to action to phase out the sale of tobacco products by 2040. Lancet 2015;385:1011-8.
10. World Health Organization Report on the Global Tobacco Epidemic 2017. Highest level of achievement in selected tobacco control measures in the 100 biggest cities in the world–Appendix IV. Available at: http://www.who.int/tobacco/global_report/2017/appendix_IV.pdf?ua=1. Accessed on 15 May 2018.
11. World Health Organization Report on the Global Tobacco Epidemic 2017. Country Report: Singapore. Available at: http://www.who.int/tobacco/surveillance/policy/country_profile/sgp.pdf. Accessed on 15 May 2018.
12. Lim TK. Singapore and the tobacco pandemic. Ann Acad Med Singapore 2008;37:363-4.
13. Clinical Practice Guideline Treating Tobacco Use and Dependence 2008 Update Panel, Liaisons, and Staff. A clinical practice guideline for treating tobacco use and dependence: 2008 update. A U.S. Public Health Service report. Am J Prev Med 2008;35:158-76.
14. Agaku IT, King BA, Dube SR. Centers for Disease Control and Prevention (CDC). Current cigarette smoking among adults, United States, 2005-2012. MMWR Morb Mortal Wkly Rep 2014;63:29-34.
15. Iestra JA, Kromhout D, van der Schouw YT, Grobbee DE, Boshuizen HC, van Staveren WA. Effect size estimates of lifestyle and dietary changes on all-cause mortality in coronary artery disease patients: a systematic review. Circulation 2005;112:924-34.
16. Bullen C. Impact of tobacco smoking and smoking cessation on cardiovascular risk and disease. Expert Rev Cardiovasc Ther 2008;6:883-95.
17. Schauer GL, Wheaton AG, Malarcher AM, Croft JB. Health-care provider screening and advice for smoking cessation among smokers with and without COPD. 2009-2010 National Adult Tobacco Survey. Chest 2016;149:676-84.
18. Cunningham P. Patient engagement during medical visits and smoking cessation counseling. JAMA Intern Med 2014;174:1291-8.

Original Article

Is Laparoscopic Sleeve Gastrectomy for Asian Super Obese a Safe and Effective Procedure?

Hannah JH Ng, [1]*MBBS*, Guowei Kim,[2]*MBBS, MMed, FRCS*, Claire Alexandra Z Chew,[2]*MBChB (Hons)*, Moe Thu San,[2]*MPH*, Jimmy BY So,[2]*MBChB, FRCSEd, MPH*, Asim Shabbir,[2]*MBBS, MMed, FRCS (Edin)*

Abstract

Introduction: Outcomes of bariatric surgery for super obese Asians are not well reported. We aimed to compare short-term outcomes of laparoscopic sleeve gastrectomy (LSG) in Asian patients with body mass index (BMI) <47.5 kg/m² to those with BMI ≥47.5 kg/m². Materials and Methods: A total of 272 patients from a Singapore university hospital who underwent LSG from 2008 to 2015 with a follow-up of at least 6 months were included in the study. Primary endpoint was weight loss at 1-year and 3-years. Morbid obesity (Group 1, G1) was defined as BMI <47.5 kg/m² and super obesity (Group 2, G2) was defined as BMI ≥47.5 kg/m². Results: There were 215 patients in G1 and 57 patients in G2 (mean preoperative weight: 107.3 kg and 146.8 kg; mean follow-up: 27.9 and 26.8 months, respectively). Mean total weight loss at 3-years of 41.9 kg for G2 was significantly higher (*P* = 0.003) than 27.2 kg for G1. Mean percentage excess weight loss (EWL) did not differ at 3-years. There was no difference in operating time, blood loss, length of stay, 30-day morbidity and readmission. There were no conversions and mortality in both groups. Remission of hypertension (*P* = 0.001) and dyslipidaemia (*P* = 0.038) were significantly associated with achieving EWL percentage (%EWL) >50 in G1. Conclusion: LSG is an equally safe and effective operation in Asians with BMI ≥47.5 kg/m² when compared to patients with BMI <47.5 kg/m² in achieving significant weight loss and improvement in comorbidities. Super obese lose more weight but have lower %EWL.

Ann Acad Med Singapore 2018;47:177-84

Key words: Short-term outcomes

Introduction

The obesity epidemic is a major public health concern worldwide. In Singapore, 8.6% of the population has a body mass index (BMI) ≥30 kg/m² and 34.3% of the population is overweight, i.e. BMI ≥25 kg/m².[1] Obesity is an independent risk factor for chronic diseases such as hypertension, dyslipidaemia and type 2 diabetes mellitus (T2DM), as well as premature death.[2,3] As a result, extensive resources and efforts are currently being allocated to search for an ideal solution to this epidemic.

Should lifestyle interventions and medical therapy fail, one possible solution for morbidly obese Asian patients (BMI ≥37.5 kg/m²), or patients with BMI ≥32.5 kg/m² with obesity-associated comorbidities, would be bariatric surgery.[4] Of the many available procedures, laparoscopic sleeve gastrectomy (LSG) has been an increasingly popular procedure globally because of the perceived ease to perform, lower morbidity and good postoperative weight loss with amelioration of comorbidities in comparison to other techniques employed.[5-9]

In Asia, reports on the difference in outcomes of LSG between super obese patients (BMI ≥47.5 kg/m²) and non-super obese patients (BMI <47.5 kg/m²) are scarce. Hence, this study aimed to examine and compare the short-term outcomes of LSG in patients with BMI <47.5 kg/m² and BMI ≥47.5 kg/m² in Singapore. The aim of our study was to

[1]Department of Surgery, Tan Tock Seng Hospital, Singapore
[2]Division of General Surgery (Upper Gastrointestinal Surgery), University Surgical Cluster, National University Hospital, Singapore
Address for Correspondence: Asst/Prof Asim Shabbir, Division of General Surgery (Upper Gastrointestinal Surgery), University Surgical Cluster, National University Hospital, Level 8 NUHS Tower Block, 1E Kent Ridge Road, Singapore 119228.
Email: cfsasim@nus.edu.sg

compare outcomes following LSG at 1- and 3-years between obese and super obese patients of Asian descent to determine if it's safe and effective for the super obese Asians.

Materials and Methods

We classified obesity as recommended by the World Health Organization (WHO), that is, a decrease by 2.5 points for each obesity category for Asians as compared to international classifications.[10] This is because Asians have a differing body composition in comparison to Caucasians, and at any given body fat percentage, Asians tend to have a lower BMI than that of Caucasians. Also, at lower BMI values, the risks for cardiovascular disease and T2DM are higher for Asians.[10] This standard has also been used in published reports of outcomes from other Asian centres.[11-13] At the 2nd Diabetes Surgery Summit, an international consensus was reached to similarly lower the BMI threshold by 2.5 kg/m^2 for Asian patients with T2DM requiring bariatric surgery.[14,15] We followed this trend in our paper.

Patients with BMI ≥32.5 kg/m^2 and with comorbidities, or BMI ≥37.5 kg/m^2 and without comorbidities—who had failed to achieve desired goals with lifestyle modifications and medical interventions—were offered bariatric surgery.

A prospective database of patients who received LSG at a university hospital in Singapore is being maintained since 2008. There were 299 patients who received LSG performed by a multidisciplinary team between August 2008 and July 2015. There are 3 bariatric surgeons in our institution, who perform approximately 100 bariatric cases combined, per year. Our technique of LSG is standardised with a 5 cm antral pouch and a gastric tube created over a 38F Bougie. Postoperatively, patients were reviewed at 2 weeks, 1 month, followed by 3-month intervals in the first year, and biannually thereafter. We strongly encourage our patients to attend support group meetings both pre and postoperatively but due to a very hectic lifestyle and time away from work, attendance at these group meetings is relatively poor.

Approval for this review of hospital records was obtained from the Institutional Review Board, DSRB NUH/2015-00002. Data for analysis on demographic, perioperative outcomes, comorbidities and weight was updated and analysed in September 2016. Twenty-seven patients were excluded from the data analysis as they did not follow-up for a minimum of ≥6 months. In total, 272 patients were grouped into BMI <47.5 kg/m^2 (Group 1, G1) or BMI ≥47.5 kg/m^2 (Group 2, G2).

The primary endpoint of our study was weight loss following LSG up to 3 years. The secondary endpoints include perioperative outcomes and the outcomes of hypertension, dyslipidaemia and T2DM at 1-year following LSG.

We followed the American Society for Metabolic and Bariatric Surgery outcome reporting standards.[16] However, we defined ideal weight by the weight corresponding to BMI 23 kg/m^2 as recommended by the WHO.[10] We also classified the complications which occurred within 30 days postoperatively according to the Clavien-Dindo classification of surgical complications.[17,18] Excess weight loss percentage (%EWL) >50 at 1-year was taken as a cutoff for successful weight loss.[19,20]

Data analysis was performed on IBM SPSS 23.0 statistical software (SPSS Inc., Chicago, IL, USA). Categorical data was presented as frequency and percentages, whereas continuous data was presented as mean and standard deviation (SD) for parametric distribution and median (interquartile range) for non-parametric distribution. For categorical data, comparisons were made by X^2 and Fisher's Exact test and for continuous data, independent-samples t test were used. For multivariate analysis, multiple linear regression was performed. A P value <0.05 was considered to be significant.

Results

There were 215 patients (79.0%) with a mean preoperative BMI of 39.3 ± 4.17 kg/m^2 in G1, and 57 patients (21.0%) with a mean preoperative BMI of 54.8 ± 6.78 kg/m^2 in G2. The characteristics of the patients are summarised in Table 1. Both groups were comparable in their mean ages, with an overall higher proportion of females. Malays formed the predominant racial group and are more likely to be super obese (P = 0.02). The mean duration of follow-up was 27.9 ± 16.6 months and 26.8 ± 16.4 months in G1 and G2, respectively.

In both groups, there were no conversions to open surgery. The mean operating time (skin-to-skin) was 112 ± 54.5 minutes (range, 30-389) and 115 ± 56.4 minutes (range, 40-352) in G1 and G2, respectively (P = 0.73). The mean intraoperative blood loss did not differ between groups and was 17.3 ± 25.0 ml and 22.3 ± 41.5 ml in G1 and G2, respectively (P = 0.41). The median length of hospital stay was 3 days in both groups. The overall total complication rates for G1 and G2 were 6.51% and 5.26%, respectively (P = 1.00). Ten patients (4.65%) in G1 had Grade I complications (P = 0.13), while 2 patients (0.93%) in G1 and 1 patient (1.75%) in G2 had Grade II complications (P = 0.51). There were 2 patients (0.93%) in G1 and 1 patient (1.75%) in G2 who had Grade III complications (P = 0.51), and 1 patient (1.75%) in G2 with Grade IV complications (P = 0.21).

The 30-day readmission rate was 6 (2.8%) in G1 and 1 (1.8%) in G2 (P = 1.00). In G1, 3 patients reported abdominal pain with vomiting, 1 patient was dehydrated, 1 patient developed Miller Fisher syndrome, and 1 patient

Table 1. Demographics

Parameter	BMI <47.5 (n = 215)	BMI ≥47.5 (n = 57)	*P* Value, 95% CI
Mean age, years ± SD	39.3 ± 11.3	39.8 ± 11.7	0.77, (-2.8, 3.8)
Range	18 – 67	17 – 61	
Gender (%)			
Male	84 (39.1)	28 (49.1)	0.18
Female	131 (60.9)	29 (50.9)	
Race (%)			
Chinese	67 (31.2)	17 (29.8)	0.02
Malay	77 (35.8)	31 (54.4)	
Indian	57 (26.5)	9 (15.8)	
Other	14 (6.5)	0 (0)	
Mean preoperative weight, kg ± SD	107.3 ± 17.3	146.8 ± 26.8	
Range	75.3 – 152	106 – 230	
Mean preoperative BMI kg/m^2, ± SD	39.3 ± 4.17	54.8 ± 6.78	
Range	32.5 – 47.4	47.6 – 79.5	
Mean number of comorbidities* ± SD	1.14 ± 1.09	1.33 ± 1.15	0.24, (-0.13, 0.52)
Hypertension (%)	99 (46.0)	32 (56.1)	0.10
Dyslipidaemia (%)	87 (40.5)	22 (38.6)	1.00
T2DM (%)	59 (27.4)	22 (38.6)	0.07

BMI: Body mass index; CI: Confidence interval; SD: Standard deviation; T2DM: Type II diabetes mellitus

*Comorbidities accounted for include hypertension, dyslipidaemia and T2DM.

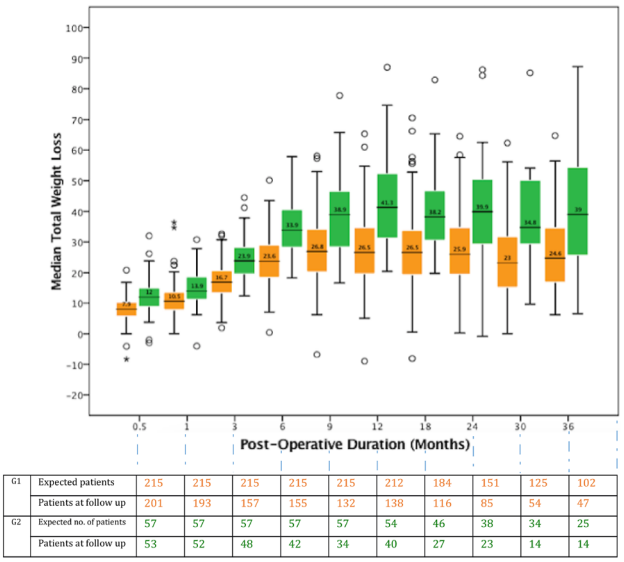

Fig. 1. Median total weight loss (TWL) trend after laparoscopic sleeve gastrectomy (LSG) in G1 (orange) and G2 (green).

Similar to TWL, the differences in mean %EWL were statistically significant in both groups at any follow-up time point up to 24 months (P >0.05), with patients in G1 having higher %EWL when compared to G2 but at 3-years, no significant difference was noted. This trend is reported in Figure 2.

At 1-year, patients in G1 were more likely to achieve successful weight loss. There were 98 patients (71.0%) in G1 as compared to 19 patients (47.5%) in G2 (P = 0.008).

suffered from early gastric stricture requiring stenting. In G2, the only readmission was due to gastroenteritis. These patients have been included in our analysis of complications.

We had no mortalities at 30-day follow-up. However, we lost 3 patients owing to medical conditions beyond 6 months follow-up. One patient died from acquired haemophilia A, another succumbed to sepsis secondary to *Klebsiella pneumoniae* urinary tract infection, and the last life lost was due to pneumonia.

The total weight loss (TWL) trends with the number of patients followed-up at all time points are shown in Figure 1. At any given point in time during follow-up, the mean TWL was significantly different between groups (P <0.05), with patients in G2 having higher TWL when compared to G1. At 1-year, median weight loss in G1 and G2 was 26.5 kg and 41.3 kg respectively (P <0.0001). Postoperatively, the weight loss stabilised at approximately 27 kg in G1, and approximately 42 kg in G2 between 9-36 months.

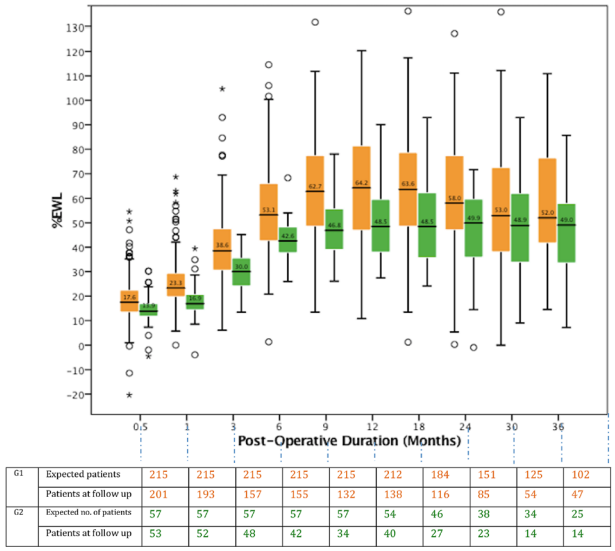

Fig. 2. %EWL trend in G1 (orange) and G2 (green).

However, in total, there were 164 patients (76.3%) in G1 and 28 patients (49.1%) in G2 who have achieved EWL >50%, irrespective of time frame ($P = 0.0001$). The trend in change in BMI (ΔBMI) and mean %TWL can be seen in Table 2.

Due to inherent differences between G1 and G2, multivariate analysis was performed, adjusting for age, gender, race and comorbidities (T2DM, hypertension and dyslipidaemia). There were significant differences between the groups in ΔBMI at all time points, with patients in G2 losing 5.83 kg/m^2 (95% CI: 2.89-8.77, P <0.001) more than G1 at 36 months postoperation. However, when multivariate analysis was performed with regard to %TWL, no significant differences were seen at all time points. These results have also been expressed in Table 2.

Table 2. ΔBMI and Mean %TWL in G1 and G2 with Multivariate Analysis

Duration (Months)	ΔBMI				Mean %TWL			
	BMI <47.5	BMI ≥47.5	Adjusted Difference*	*P* Value	BMI <47.5	BMI ≥47.5	Adjusted Difference*	*P* Value
0.5	2.9 ± 1.3	4.7 ± 2.6	1.73 (1.21 – 2.25)	<0.001	8.1 ± 3.7	9.3 ± 4.3	0.95 (-0.24 – 2.14)	0.118
1	4.0 ± 1.6	5.6 ± 2.6	1.58 (1.03 – 2.12)	<0.001	11.4 ± 4.7	11.4 ± 4.7	-0.21 (-1.62 – 1.20)	0.770
3	6.4 ± 1.9	9.3 ± 2.7	2.92 (2.23 – 3.62)	<0.001	19.6 ± 6.7	20.5 ± 5.6	1.01 (-1.15 – 3.17)	0.358
6	8.7 ± 2.5	12.9 ± 2.7	4.22 (3.37 – 5.08)	<0.001	29.0 ± 10.0	31.9 ± 7.3	3.12 (-0.11 – 6.34)	0.059
9	10.0 ± 3.3	15.0 ± 4.7	4.85 (3.53 – 6.18)	<0.001	35.0 ± 13.9	37.7 ± 12.8	2.70 (-2.25 – 7.65)	0.283
12	10.2 ± 4.0	15.7 ± 5.2	5.67 (4.21 – 7.12)	<0.001	36.5 ± 17.7	41.7 ± 17.0	5.73 (-0.12 – 11.58)	0.055
18	10.2 ± 4.2	16.0 ± 7.4	5.96 (3.90 – 8.01)	<0.001	37.2 ± 19.0	43.8 ± 26.3	7.74 (-0.72 – 16.20)	0.073
24	10.1 ± 4.0	15.3 ± 7.3	5.70 (3.43 – 7.96)	<0.001	35.9 ± 17.8	39.2 ± 18.7	5.55 (-2.80 – 13.90)	0.191
30	9.2 ± 4.3	15.7 ± 8.4	6.50 (3.06 – 9.95)	<0.001	31.8 ± 19.5	43.9 ± 33.7	8.99 (-5.62 – 23.60)	0.223
36	9.6 ± 4.3	15.3 ± 7.2	5.83 (2.89 – 8.77)	<0.001	34.6 ± 20.1	40.9 ± 24.0	7.90 (-3.68 – 19.48)	0.177

BMI: Body mass index; G1: Group 1; G2: Group 2; %TWL: Percentage of total weight loss
*Multivariate analysis adjusting for age, gender, race, hypertension, T2DM, dyslipidaemia.

At 1-year postoperation, both groups experienced a significant reduction in mean number of comorbidities, from 1.14 ± 1.09 to 0.65 ± 0.92 in G1 (P <0.0001), and 1.33 ± 1.15 to 0.70 ± 0.93 in G2 (P <0.0001).

Remission rates of hypertension, dyslipidaemia and T2DM were similar among groups at 1-year, though this did not achieve statistical significance. Remission of hypertension was achieved in 18 patients (18.2%) and 5 patients (15.6%) in G1 and G2, respectively ($P = 1.00$). There were a higher proportion of patients with a remission of dyslipidaemia in patients in G1, with 26 patients (29.9%) as compared to 4 patients (18.2%) in patients in G2 ($P = 0.56$). Remission of T2DM was recorded in 20 patients (33.9%) in G1 and 12 patients (54.5%) in G2 ($P = 0.27$).

Successful weight loss (%EWL >50) was associated with remission of hypertension ($P = 0.001$) and dyslipidaemia ($P = 0.038$) in G1. In patients with remission of hypertension, 15 (34.1%) achieved successful weight loss as compared to 1 patient (3.2%) who failed to achieve successful weight loss. In patients with remission of dyslipidaemia, 17 patients (34.0%) achieved successful weight loss as compared to 2 patients (9.5%) who failed to achieve successful weight loss.

For patients in G2, no significant difference ($P = 0.60$) was found in the remission rates of hypertension in patients who achieved successful weight loss (1 patient, 9.1%) and those who did not (3 patients, 21.4%). Also, no significant difference ($P = 0.52$) was found in the remission rate of dyslipidaemia in patients who achieved successful weight loss (2 patients, 28.6%) and those who did not (1 patient, 11.1%).

Remission of T2DM in both groups was not related to successful weight loss at 1-year. This can be seen in Table 3. The absolute value of TWL was not associated with remission of comorbidities. This can be seen in Table 4.

Discussion

LSG has been gaining traction as the operation of choice for bariatric patients as it is accepted as a safe and effective procedure.[21-23] It was originally introduced as a bridging procedure for the super obese than as a primary outcome.[24]

However, there is a paucity of Asian literature comparing the outcomes of LSG between patients with different BMI categories. The increasing trend towards the widespread use of this procedure thus requires a careful evaluation of its safety and efficacy, especially in super obese patients.

Singapore has a population of 5.54 million indigenous people, out of which 3.90 million are Singapore citizens.

Table 3. Remission of Comorbid Conditions as a Comparison to %EWL

Parameter	BMI <47.5			BMI ≥47.5		
	%EWL <50	%EWL >50	*P* Value	%EWL <50	%EWL >50	*P* Value
Hypertension (%)	n = 31	n = 44	0.001	n = 9	n = 7	0.52
Remission	1 (3.2)	15 (34.1)		1 (11.1)	2 (28.6)	
No remission	26 (83.9)	26 (59.1)		6 (66.7)	3 (42.9)	
Patients excluded*	4 (12.9)	3 (6.8)		2 (14.3)	2 (18.2)	
Dyslipidaemia (%)	n = 21	n = 50	0.038	n = 9	n = 7	0.52
Remission	2 (9.5)	17 (34.0)		1 (11.1)	2 (28.6)	
No remission	16 (76.2)	27 (54.0)		6 (66.7)	3 (42.9)	
Patients excluded*	3 (14.3)	6 (12.0)		2 (22.2)	2 (28.6)	
T2DM (%)	n = 18	n = 24	0.096	n = 10	n = 8	0.63
Remission	4 (22.2)	12 (50.0)		7 (70.0)	4 (50.0)	
No remission	11 (61.1)	9 (37.5)		2 (20.0)	2 (25.0)	
Patients excluded*	3 (16.7)	3 (12.5)		1 (10.0)	2 (25.0)	

BMI: Body mass index; %EWL: Percent of excess weight loss; T2DM: Type II diabetes mellitus

*Patients excluded are those patients whose 1-year (post-LSG) blood pressures, lipid panel and HbA1c were unable to be obtained.

Table 4. TWL at 1-year in Comparison to Remission of Comorbidities

Parameter	TWL 0 – 20 kg n = 37	TWL 20 – 40 kg n = 96	TWL 40 – 60 kg n = 39	TWL >60 kg n = 64	*P* Value
Hypertension (%)	n = 27	n = 49	n = 20	n = 35	0.14
Remission	4 (14.8)	9 (18.4)	6 (30.0)	3 (8.6)	
No remission	20 (74.1)	38 (77.6)	9 (45.0)	25 (71.4)	
Patients excluded*	3 (11.1)	2 (4.1)	5 (25.0)	7 (20.0)	
Dyslipidaemia (%)	n = 22	n = 53	n = 10	n = 22	0.79
Remission	4 (18.2)	14 (26.4)	3 (30.0)	4 (18.2)	
No remission	14 (63.6)	33 (62.3)	5 (50.0)	14 (63.6)	
Patients excluded*	4 (18.2)	6 (11.3)	2 (20.0)	4 (18.2)	
T2DM (%)	n = 19	n = 29	n = 11	n = 16	0.15
Remission	5 (26.3)	15 (51.7)	6 (54.5)	6 (37.5)	
No remission	12 (63.2)	9 (31.0)	3 (27.3)	6 (37.5)	
Patients excluded*	2 (10.5)	5 (17.2)	2 (18.2)	4 (25.0)	

TWL: Total weight loss; T2DM: Type II diabetes mellitus

*Patients excluded are those patients whose 1-year (post-LSG) blood pressures, lipid panel and HbA1c were unable to be obtained.

The ethnic distribution of Singapore citizens is 74.3% Chinese, 13.3% Malay, 9.1% Indian and 3.3% other minority racial groups, such as Eurasians.[25] In 2010, 10.8% of the population was obese in Singapore, as compared to 35.7% of the population in America, suggesting that the prevalence of obesity is not as high in Singapore.[26] However, this trend is only set to rise as a result of the global obesity epidemic. Correspondingly, the popularity of bariatric surgery has only recently experienced an uptrend. Overall in Singapore, approximately 350 bariatric procedures are performed annually and despite our small number of patients, our centre is one of the high volume centres. Despite being a minority racial group in Singapore, Malays made up a high proportion of our patient population (39.7%) and Malays were more likely to have a BMI >47.5 kg/m^2 (P = 0.02). This is similar to Singapore's obesity prevalence in racial group distributions, where Malays were more likely to be obese, and a higher proportion of Malays were obese as compared to the other racial groups.[27] An explanation for this phenomenon could be due to cultural differences, as Malay cuisine is generally higher in saturated fat. Another possibility could be the lower socioeconomic status of Malays. However, no studies have been conducted to explore the causes for this disparity.

We also noted that super obese patients did not have more comorbidities as compared to obese patients. There were no differences in mean number of comorbidities between G1 and G2, with 1.14 ± 1.09 in G1 and 1.33 ± 1.15 in G2 (P = 0.24). We postulated that our relatively young patient population could have contributed to this trend.

In literature, it has been reported that LSG has a lower complication rate than other bariatric surgeries.[28,29] It has also been reported that LSG is safe as a treatment for the super obese.[30] Similarly, we found that LSG is equally safe in patients with BMI = 47.5 kg/m^2. There was no difference in the overall complication rate in both groups (4.65% in G1 and 5.26% in G2 [P = 1.00]) and within each grade of complication in the Clavien-Dindo classification.[17,18] The majority of our complications fell into Grade I complications, followed by Grade II complications. The 2 patients in G1 with Grade III complications were due to an iatrogenic bowel perforation and the patient subsequently underwent a laparoscopic washout with suture repair (on postoperative day 2) and an early gastric tube stricture (which was treated with endoscopic stent insertion). The patient in G2 with Grade III complication was due to fluid collection necessitating drainage. The patient in G2 with Grade IV complication was due to type 2 respiratory failure who required intubation. All patients with Grade III and Grade IV complications subsequently recovered and there was no surgical mortality in our series up to 6 months. Additionally, we found no significant difference in intraoperative outcomes, length of hospital stay and readmission rate between both groups. Our operative times in both groups are reported in terms of skin-to-skin time and are deceptively long. We say this because we are involved in clinical and basic science research projects that necessitate specimen collection intraoperatively like omental fat and muscle biopsies, thus prolonging the operative time.

Overall, our study added evidence to support that LSG is an equally safe procedure in the super obese in comparison to the obese. Super obese patients should not be excluded from LSG because of a perceived risk based on BMI.

Consistent with literature, our results suggested that LSG was effective in achieving substantial weight reduction over short-term follow-up.[31-34] The mean %TWL of 36.5 ± 17.7 and 41.7 ± 17.0 at 1-year, 35.9 ± 17.8 and 39.2 ± 18.7 at 2-years, and 34.6 ± 20.1 and 40.9 ± 24.0 at 3-years in patients with BMI <47.5 kg/m^2 and BMI ≥47.5 kg/m^2, respectively.

However, although LSG has been suggested as a reliable bariatric procedure, several studies have shown that there is a difference in the efficacy of LSG in patients with different BMIs.[35,36] Junior et al found that patients with a higher BMI lost more %TWL in 48 months, with %EWL lower than that or equal to less heavy patients due to their much greater excess weight preoperatively.[37] In our series, our 3-year outcomes similarly revealed that patients with BMI ≥47.5 kg/m^2 have a higher quantum of TWL despite a lower mean %EWL as compared to patients with BMI <47.5 kg/m^2. The mean TWL was 27.7 ± 12.2 kg and 42.2 ± 15.2 kg at 1-year, 27.2 ± 12.5 kg and 41.3 ± 20.1 kg at 2-years, and 26.8 ± 13.6 kg and 41.9 ± 21.6 kg at 3-years in patients with BMI <47.5 kg/m^2 and BMI ≥47.5 kg/m^2, respectively.

We also found that despite a higher quantum of TWL in patients in G2 as compared to patients in G1 where the difference was significant at all time points (P<0.05), %TWL at 1-, 2- and 3-year time points were similar between both groups (P >0.05). We believe that because patients who are super obese do not perform inferiorly to patients who are obese in terms of %TWL, there could be a set point involved in the percentage of weight an individual could stand to lose from intervention.[38]

Further, success of surgery (defined as %EWL >50) is an accepted benchmark and currently the only benchmark. This is because %TWL has only been recently introduced as an outcome to be measured and reported, and there is no widely accepted benchmark of %TWL to indicate success of surgery.[19,20,39] Our 1-year %EWL >50 were 71% in G1 versus 47.5% in G2 (P = 0.008), demonstrating that patients in G1 were more likely to achieve surgical success. Postulating that super obese patients required a longer duration to achieve surgical success, we analysed %EWL >50 at 1-year in G1 verses %EWL >50 at 1.5-years and 2-years in G2. Patients in G1 were still more likely to achieve surgical success at 1-year versus 1.5-years in G2 (P = 0.026) and versus 2-years in G2 (P = 0.033). We further analysed success of surgery (irrespective of time frame). Overall, patients in G1 were still more likely to achieve surgical success (P = 0.0001). Conversely, this meant that patients in G2 were more likely to achieve surgical failure. Boza et al similarly reported a higher percentage of patients in lower BMI categories achieving surgical success.[40]

As a result, we propose that the definition of surgical failure should differ between morbid and super obesity. %EWL is not a good measure to compare weight loss as the findings from TWL appear to be converse to those from %EWL, with the super obese requiring a higher quantum of TWL to achieve similar %EWL.[35] This can be attributed to the higher initial weight of patients with BMI ≥47.5 kg/m^2. To achieve similar %EWL for patients in both groups, patients with BMI ≥47.5 kg/m^2 would have to achieve a higher TWL in order to come close to their ideal body weight when compared to patients with BMI <47.5 kg/m^2. Additionally, there may be greater impact of baseline weight on %EWL than on TWL. We note that recent studies have included %TWL in outcome reporting after a bariatric procedure.[41,42] We similarly propose that on top of reporting %EWL, TWL should be included as a compulsory measure of reporting.

As there is no standard definition for success of surgery for patients in different BMI categories, more research is needed to define an acceptable and fair benchmark.

LSG is known to have a great impact on comorbidities, narrated in a systemic review by Shi et al.[43] Apart from weight control, our results also demonstrated the resolution of obesity-associated comorbidities at 1-year after LSG in both groups, with 18.2% and 15.6% for remission of hypertension, 29.9% and 18.2% for remission of dyslipidaemia, and 33.9% and 54.5% for remission of T2DM for patients in G1 and G2, respectively. From our analysis, the quantum of TWL was not associated with remission of comorbidities. No significant differences in rates of resolution of comorbidities were observed between the groups (P >0.05), and this could suggest that LSG is equally effective in its impact in resolution of comorbidities in both the super obese and obese Asian patients. We also observed that patients who had a BMI <47.5 kg/m^2 and who achieved successful weight loss of %EWL >50 were significantly associated with remission of hypertension and dyslipidaemia. This suggests that adequate weight loss is important to achieve remission of hypertension and dyslipidaemia after LSG in patients with a lower BMI.

More importantly, our results demonstrate the reduction in the mean number of comorbidities at 1-year after LSG in both groups, with preoperative mean number of comorbidities at 1.14 ± 1.09 in G1 and 1.33 ± 1.15 in G2, and postoperative mean number of comorbidities at 0.65 ± 0.92 (P <0.0001) in G1 and 0.70 ± 0.93 (P <0.0001) in G2. In concordance with literature, this suggests that LSG in our series is effective in ameliorating comorbidities in both super obese and obese Asian patients.[44]

There are several limitations to our study. The first is the small sample size of patients who are super obese (57 patients). This is due to the small number of super obese in Asia. Also, Singapore has a small population size, and bariatric surgery is a relatively new subspecialty in Singapore, thus there is low awareness of this treatment modality. The second limitation is the considerable loss of patients to follow-up at 3-years (at 52.6% for patients with BMI <47.5 kg/m^2, and 56.1% for patients with BMI ≥47.5 kg/m^2). This may cause bias in outcomes as patients with poor outcomes and equally those with excellent outcomes may have been lost to follow-up. This is because patients perceive themselves to be well, and they are not keen for follow-up. However, we are mitigating this by trying to reach out to these patients to grow our data pool. The third limitation of our study is that our study is retrospective in nature. However, all data were taken from a prospective database and we included all consecutive patients who had at least 6 months of follow-up to reduce reporting bias. Finally, we only examined short-term outcomes, and a longer duration of follow-up is required to further support our results. We aim to revisit this when we have the optimum number of patients.

Conclusion

LSG is an equally safe and effective weight loss procedure for super obese Asian patients when compared to obese Asian patients. Asian patients with BMI ≥47.5 kg/m^2 should be considered as acceptable candidates for LSG.

REFERENCES

1. Obesity. Health Promotion Board. HPB-MOH Clinical Practice Guidelines 2016. Available at: https://www.hpb.gov.sg/docs/default-source/pdf/obesity-cpg_main_for-online-30-aug.pdf?sfvrsn=2288eb72_0. Accessed on 8 August 2017.
2. Bassett J. International Diabetes Institute; World Health Organization Regional Office for the Western Pacific; International Association for the Study of Obesity; International Obesity Task Force. The Asia-Pacific perspective: redefining obesity and its treatment. Melbourne: Health Communications Australia; 2000.
3. Zheng W, McLerran DF, Rolland B, Zhang X, Inoue M, Matsuo K, et al. Association between body-mass index and risk of death in more than 1 million Asians. N Engl J Med 2011;364:719-29.
4. Goel R, Agarwal A, Shabbir A, So JB, Pasupathy S, Wong A, et al. Bariatric surgery in Singapore from 2005 to 2009. Asian J Surg 2013;36:36-9.
5. Abbatini F, Rizzello M, Casella G, Alessandri G, Capoccia D, Leonetti F, et al. Long-term effects of laparoscopic sleeve gastrectomy, gastric bypass, and adjustable gastric banding on type 2 diabetes. Surg Endosc 2010;24:1005-10.
6. Akkary E, Duffy A, Bell R. Deciphering the sleeve: technique, indications, efficacy, and safety of sleeve gastrectomy. Obes Surg 2008;18:1323-9.
7. Angrisani L, Santonicola A, Iovino P, Formisano G, Buchwald H, Scopinaro N. Bariatric surgery worldwide 2013. Obes Surg 2015;25:1822-32.
8. Himpens J DG, Cadière GB. A prospective randomized study between laparoscopic gastric banding and laparoscopic isolated sleeve gastrectomy: results after 1 and 3 years. Obes Surg 2006;16:1450-6.
9. Young MT, Gebhart A, Phelan MJ, Nguyen NT. Use and outcomes of laparoscopic sleeve gastrectomy vs laparoscopic gastric bypass: analysis of the American College of Surgeons NSQIP. J Am Coll Surg 2015;220:880-5.
10. World Health Organization Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363:157-63.
11. Ching SS, Cheng AK, Kong LW, Lomanto D, So JB, Shabbir A. Early outcomes of laparoscopic sleeve gastrectomy in a multiethnic Asian cohort. Surg Obes Relat Dis 2016;12:330-7.
12. Park JY, Kim YJ. Laparoscopic roux-en-Y gastric bypass in obese Korean patients: efficacy and potential adverse events. Surg Today 2016;46:348-55.
13. Prasad P, Tantia O, Patle N, Khanna S, Sen B. An analysis of 1-3-year follow-up results of laparoscopic sleeve gastrectomy: an Indian perspective. Obes Surg 2012;22:507-14.
14. Rubino F, Nathan DM, Eckel RH, Schauer PR, Alberti KG, Zimmet PZ, et al. Metabolic surgery in the treatment algorithm for type 2 diabetes: a

joint statement by international diabetes organizations. Surg Obes Relat Dis 2016;12:1144-62.

15. Rubino F, Nathan DM, Eckel RH, Schauer PR, Alberti KG, Zimmet PZ, et al. Metabolic surgery in the treatment algorithm for type 2 diabetes: a joint statement by international diabetes organizations. Diabet Care 2016;39:861-77.
16. Brethauer SA, Kim J, el Chaar M, Papasavas P, Eisenberg D, Rogers A, et al. Standardized outcomes reporting in metabolic and bariatric surgery. Surg Obes Relat Dis 2015;11:489-506.
17. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-13.
18. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, et al. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 2009;250:187-96.
19. Hirth DA, Jones EL, Rothchild KB, Mitchell BC, Schoen JA. Laparoscopic sleeve gastrectomy: long-term weight loss outcomes. Surg Obes Relat Dis 2015;11:1004-7.
20. Palmisano S, Silvestri M, Giuricin M, Baldini E, Albertario S, Capelli P, et al. Preoperative predictive factors of successful weight loss and glycaemic control 1 year after gastric bypass for morbid obesity. Obes Surg 2015;25:2040-6.
21. ASMBS Clinical Issues Committee. Updated position statement on sleeve gastrectomy as a bariatric procedure. Surg Obes Relat Dis 2012;8:e21-6.
22. Rosenthal RJ, International Sleeve Gastrectomy Expert P, Diaz AA, Arvidsson D, Baker RS, Basso N, et al. International Sleeve Gastrectomy Expert Panel Consensus Statement: best practice guidelines based on experience of >12,000 cases. Surg Obes Relat Dis 2012;8:8-19.
23. Albanopoulos K, Tsamis D, Natoudi M, Alevizos L, Zografos G, Leandros E. The impact of laparoscopic sleeve gastrectomy on weight loss and obesity-associated comorbidities: the results of 3 years of follow-up. Surg Endosc 2016;30:699-705.
24. Milone L, Strong V, Gagner M. Laparoscopic sleeve gastrectomy is superior to endoscopic intragastric balloon as a first stage procedure for super-obese patients (BMI ≥50). Obes Surg 2005;15:612-7.
25. Singapore MOH. Population and Vital Statistics, 2016. Available at: https://www.moh.gov.sg/content/moh_web/home/statistics/Health_Facts_Singapore/Population_And_Vital_Statistics.html. Accessed on 8 August 2017.
26. Flegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among us adults, 1999-2010. JAMA 2012;307:491-7.
27. Epidemiology & Disease Control Division, Ministry of Health. National Health Survey 2010. Available at: https://www.moh.gov.sg/content/dam/moh_web/Publications/Reports/2011/NHS2010%20-%20low%20res.pdf. Accessed on 8 August 2017.
28. Dogan K, Gadiot RP, Aarts EO, Betzel B, van Laarhoven CJ, Biter LU, et al. Effectiveness and safety of sleeve gastrectomy, gastric bypass and adjustable gastric banding in morbidly obese patients: a multicenter, retrospective, matched cohort study. Obes Surg 2015;25:1110-8.
29. Zhang Y, Ju W, Sun X, Cao Z, Xinsheng X, Daquan L, et al. Laparoscopic sleeve gastrectomy versus laparoscopic roux-en-Y gastric bypass for morbid obesity and related comorbidities: a meta-analysis of 21 studies. Obes Surg 2015;25:19-26.
30. Falk V, Twells L, Gregory D, Murphy R, Smith C, Boone D, et al. Laparoscopic sleeve gastrectomy at a new bariatric surgery centre in Canada: 30-day complication rates using the Clavien-Dindo classification. Can J Surg 2016;59:93-7.
31. Hamoui N, Anthone GJ, Kaufman HS, Crookes PF. Sleeve gastrectomy in the high-risk patient. Obes Surg 2006;16:1445-9.
32. Liu SY, Wong SK, Lam CC, Yung MY, Kong AP, Ng EK. Long-term results on weight loss and diabetes remission after laparoscopic sleeve gastrectomy for a morbidly obese Chinese population. Obes Surg 2015;25:1901-8.
33. Mui WL, Ng EK, Tsung BY, Lam CC, Yung MY. Laparoscopic sleeve gastrectomy in ethnic obese Chinese. Obes Surg 2008;18:1571-4.
34. Wang X, Chang XS, Gao L, Zheng CZ, Zhao X, Yin K, et al. Effectiveness of laparoscopic sleeve gastrectomy for weight loss and obesity-associated co-morbidities: a 3-year outcome from Mainland Chinese patients. Surg Obes Relat Dis 2016;12:1305-11.
35. Alexandrou A, Felekouras E, Giannopoulos A, Tsigris C, Diamantis T. What is the actual fate of super-morbid-obese patients who undergo laparoscopic sleeve gastrectomy as the first step of a two-stage weight-reduction operative strategy? Obes Surg 2012;22:1623-8.
36. Tagaya N, Kasama K, Kikkawa R, Kanahira E, Umezawa A, Oshiro T, et al. Experience with laparoscopic sleeve gastrectomy for morbid versus super morbid obesity. Obes Surg 2009;19:1371-6.
37. Junior WS, Campos CS, Nonino CB. Reporting results after bariatric surgery: reproducibility of predicted body mass index. Obes Surg 2012;22:519-22.
38. Farias MM, Cuevas AM, Rodriguez F. Set-point theory and obesity. Metab Syndr Relat Disord 2011;9:85-9.
39. Baltasar A, Bou R, Bengochea M, Arlandis F, Escriva C, Miro J, et al. Duodenal switch: an effective therapy for morbid obesity–intermediate results. Obes Surg 2001;11:54-8.
40. Boza C, Daroch D, Barros D, Leon F, Funke R, Crovari F. Long-term outcomes of laparoscopic sleeve gastrectomy as a primary bariatric procedure. Surg Obes Relat Dis 2014;10:1129-33.
41. Seki Y, Kasama K, Hashimoto K. Long-term outcome of laparoscopic sleeve gastrectomy in morbidly obese Japanese patients. Obes Surg 2016;26:138-45.
42. Lemanu DP, Srinivasa S, Singh PP, MacCormick AD, Ulmer S, Morrow J, et al. Single-stage laparoscopic sleeve gastrectomy: safety and efficacy in the super-obese. J Surg Res 2012;177:49-54.
43. Shi X, Karmali S, Sharma AM, Birch DW. A review of laparoscopic sleeve gastrectomy for morbid obesity. Obes Surg 2010;20:1171-7.
44. Moon RC, Nelson L, Teixeira AF, Jawad MA. Outcomes of Roux-en-Y gastric bypass in the super obese: comparison of body mass index 50-60 kg/m^2 and ≥60 kg/m^2 with the morbidly obese. Surg Obes Relat Dis 2016;12:292-6.

Commentary

Yellow Fever – What It Means for Singapore

Glorijoy SE Tan, [1]*MBBS, MCRP (UK), MMed (Int Med)*, Monica Chan,[1]*BMBS (Hons), MRCP (UK), MCI*, Poh Lian Lim, [1,2]*MD, MPH, FAMS*

Yellow fever (YF) is an arthropod-borne viral haemorrhagic disease transmitted by *Aedes aegypti* and *Hemagogus* mosquitoes, belonging to the flavivirus family which includes dengue, Zika and West Nile virus. Infected persons may have symptoms that range from subclinical infection to multi-organ failure and death. In contrast to dengue which has a low mortality rate of approximately 1%, case-fatality ratio of YF is 20%-50% among the approximately 15% of infected persons who develop severe disease.[1] Fortunately, YF can be prevented using a live vaccine which confers lifelong protection 10 days after the vaccine is administered. The international certificate of vaccination or prophylaxis is issued by the World Health Organization (WHO) to a person who has been vaccinated. It is valid for life, and may be a requirement for entry to certain countries under International Health Regulations (IHR).[2]

YF is endemic in the tropical regions of South America and sub-Saharan Africa, and is estimated to cause up to 60,000 deaths worldwide every year.[3] A succession of recent outbreaks has highlighted the propensity for YF to spread to urban areas and other geographic regions. In December 2015, a large urban outbreak of YF occurred in Angola with subsequent spread to Democratic Republic of Congo (DRC), resulting in 962 confirmed cases (884 in Angola and 78 in DRC) and emergency vaccination of over 30 million persons.[4] The shortage of emergency vaccine stockpile prompted health authorities to immunise inhabitants with one-fifth of the standard dose to extend the vaccine supply. This outbreak spread to other countries including Kenya and resulted in the first ever cases of YF in Asia.[5] In March 2016, 11 imported YF cases were reported in travellers returning to China from Angola, despite the requirement by China for proof of vaccination under IHR. Although no local transmission subsequently occurred, this represented a potentially catastrophic event of YF introduction into a large unvaccinated population.

Soon after the WHO announcement in February 2017 declaring the end of the year-long YF epidemic in Africa, Brazil reported the worst epidemic of YF seen in decades. The earliest cases were first reported from the State of Minas Gerais as early as December 2016,[6] followed by continued expansion towards the Atlantic coast of the country and closer to more densely populated areas of Rio de Janeiro. As of July 2017, there have been 3240 suspected cases reported with an overall case fatality rate of 35% among confirmed cases.[7] In response to the ongoing outbreak, health authorities and the Brazilian Ministry of Health have conducted mass vaccination campaigns among residents in affected areas. In order to do so, Brazil requested 3.5 million doses of YF vaccine from global emergency stockpile managed by the International Coordinating Group (ICG) on Vaccine Provision for YF.[8]

Efforts to curb the spread of YF were hampered by the shortage of vaccines. Globally, YF vaccines continue to be in short supply due to pharmaceutical manufacturing problems, and the world's emergency vaccine stockpile faces impending depletion in the face of the Brazil outbreak. In the United States (US), there are ongoing efforts to import and use an alternative YF vaccine from an external source[9] and the US Centers for Disease Control and Prevention (CDC) has issued a Level 2 travel alert recommending enhanced precautions to be taken prior to travel to affected areas.[10]

This current outbreak of YF in Brazil is disturbingly reminiscent of the Zika virus epidemic that spread across the Americas.[11] Singapore reported the first laboratory-confirmed Zika virus infection in April 2016 in a business traveller who returned from Brazil. National preparedness plans were in place, and initial efforts at containment included intensive vector control and mandatory hospital quarantine. However, subsequent clusters of Zika were detected, and Zika has now become a sporadic viral infection in Singapore.

The ongoing outbreak of YF in Brazil presents a serious public health risk for Singapore. Singapore receives over 50,000 travellers from the Americas every year, far higher than the 8000 travellers who arrive from Africa.[12] YF infection results in viraemia, which may persist for up to 5 days. The prospect of a viraemic patient being bitten by a competent vector, and causing onward autochthonous spread into an almost completely unvaccinated population

[1]Department of Infectious Diseases, Institute of Infectious Diseases and Epidemiology, Tan Tock Seng Hospital, Singapore
[2]Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore
Address for Correspondence: Dr Glorijoy Tan Shi En, Department of Infectious Diseases, Institute of Infectious Diseases and Epidemiology, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433.
Email: glorijoy.tan@mohh.com.sg

is the scenario being contemplated. Local ecology, high volume of international travel, low vaccine coverage and an overlapping clinical syndrome with other endemic infections are prime conditions for a potentially devastating outbreak in Asia.[13]

Healthcare facilities in Singapore are expected to be fully capable of assessing a returning traveller with transmissible infections. Building on experience preparing for Ebola and Zika, YF preparedness measures have been put in place at national and hospital levels. These include enhancing laboratory diagnostic capability, clinical protocols, surveillance systems, 'One Health' collaborations with environmental agencies involved in vector control and plans to make YF vaccines available. The challenge lies in the broad range of differential diagnoses, including other viral haemorrhagic fevers, in an ill returning traveller from South America or sub-Saharan Africa. This increases the risk that an actual case of YF would go undiagnosed or mistaken for another non-specific febrile illness. Such an individual would be capable of spreading YF to local mosquitoes during the period of viraemia.

If local urban transmission of YF occurs in Singapore, and serological evidence subsequently demonstrates circulation in primate populations, Singapore could conceivably join the list of countries with documented YF transmission. Despite the availability of effective vaccination, persons in whom the YF vaccination is contraindicated or to be used with caution—such as immunocompromised persons, pregnant women, and infants under 9 months—could remain susceptible to YF infections acquired locally. Such a development, which is possible although currently improbable, would have far-reaching clinical, public health and economic repercussions. This would also adversely impact Singapore's hard-earned status as a major international hub for trade and travel, for increased restrictions would be enforced upon persons travelling to and from the country under the IHR.

Singapore requires YF vaccination of all travellers entering Singapore from countries with documented YF transmission, and isolation of suspected cases can be mandated under the Infectious Disease Act. Aggressive vector control, ring vaccination protocols, quarantine and personal protective measures would be important strategies to activate if the first case of YF is detected in Singapore.

Despite all the factors that make the transmission of YF conducive in Asia, a possible explanation for its absence thus far is the hypothesis that cross-reactive dengue antibodies confer partial protective immunity to YF, in a region where dengue is endemic.[14]

In a health survey to understand health-seeking behaviour of Singaporeans attending a travel health clinic, it was found that less than 20% of them had consulted a doctor before prior travel experience, and less than 70% of those who consulted a doctor before travel received pretravel or vaccination advice.[15] The low rates of pretravel consultation is an area that may be focused on in improving destination-related vaccination uptake and travel precautions to mitigate the risks of infectious disease importation into Singapore.

With increased globalisation, Singapore will always be potentially vulnerable to the threat of infectious diseases that are imported as a result of international travel. Ongoing vigilance, strict adherence to international guidelines and investments in preparedness strategies are our safeguards against the risk of a YF outbreak in Singapore.

REFERENCES

1. Staples JE, Gershman M, Fischer M. Yellow fever vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2010;59:1-27.
2. World Health Organization. International Health Regulations (2005). 3rd Edition. Available at: http://apps.who.int/iris/bitstream/10665/246107/1/9789241580496-eng.pdf?ua=1. Accessed on 10 October 2017.
3. World Health Organization. Yellow Fever. Fact sheet. May 2016. Available at: http://www.who.int/mediacentre/factsheets/fs100/en/. Accessed on 7 May 2017.
4. World Health Organization. Yellow fever outbreak: Angola, Democratic Republic of the Congo and Uganda, 2016-2017. Available at: http://www.who.int/emergencies/yellow-fever/en/. Accessed on 17 October 2017.
5. Ling Y, Chen J, Huang Q, Hu Y, Zhu A, Ye S, et al. Yellow fever in a worker returning to China from Angola, March 2016. Emerg Infect Dis 2016;22:1317-8.
6. World Health Organization. Yellow fever – Brazil 13 January 2017. Available at: http://www.who.int/csr/don/13-january-2017-yellow-fever-brazil/en/. Accessed on 7 May 2017.
7. Organization PAHOWH. Epidemiological Update: Yellow Fever, Washington, DC, 10 July 2017. Available at: http://www.paho.org/hq/index.php?option=com_docman&task=doc_download&Itemid=270&gid=41102&lang=en. Accessed on 17 October 2017.
8. World Health Organization. WHO dispatched 3.5 million doses of yellow fever vaccine for outbreak response in Brazil 2017. Available at: http://www.who.int/csr/disease/yellowfev/vaccination-in-Brazil/en/. Accessed on 17 November 2017.
9. Gershman MD, Angelo KM, Ritchey J, Greenberg DP, Muhammad RD, Brunette G, et al. Addressing a yellow fever vaccine shortage - United States, 2016-2017. MMWR Morb Mortal Wkly Rep 2017;66:457-9.
10. CDC. Yellow Fever in Brazil, 2017. Available at: https://wwwnc.cdc.gov/travel/notices/alert/yellow-fever-brazil. Accessed on 17 November 2017.
11. Hennessey M, Fischer M, Staples JE. Zika virus spreads to new areas - region of the americas, May 2015-January 2016. MMWR Morb Mortal Wkly Rep 2016;65:55-8.

12. Board ST. International Visitor Arrivals, 2016. Available at: https://www.stb.gov.sg/statistics-and-market-insights/Pages/statistics-Visitor-Arrivals.aspx. Accessed on 7 May 2017.
13. Wasserman S, Tambyah PA, Lim PL. Yellow fever cases in Asia: primed for an epidemic. Int J Infect Dis 2016;48:98-103.
14. Izurieta RO, Macaluso M, Watts DM, Tesh RB, Guerra B, Cruz LM, et al. Anamnestic iummune response to dengue and decreased severity of yellow fever. J Glob Infect Dis 2009;1:111-6.
15. Lee VJ, Wilder-Smith A. Travel characteristics and health practices among travellers at the travellers' health and vaccination clinic in Singapore. Ann Acad Med Singapore 2006;35:667-73.

Letter to the Editor

An Initial Experience Comparing Robotic Total Mesorectal Excision (RTME) and Transanal Total Mesorectal Excision (taTME) for Low Rectal Tumours

Dear Editor,

Laparoscopic surgery is widely used for the surgical treatment of rectal cancer. However, very low rectal cancer presents with special difficulty. Laparoscopic dissection beyond a protruding sacral promontory, especially in a small confined pelvic space in a fat male pelvis, is technically difficult. This is where the use of the robotic total mesorectal resection (RTME) is thought to be useful. In more recent times, transanal total mesorectal excision (taTME) promises to bring about another novel solution to this issue. Hence, we compared our initial cases of RTME and taTME to assess surgical parameters between these 2 procedures, as a guide to others embarking on these same techniques.

Materials and Methods

The first 21 consecutive patients who underwent RTME using the da Vinci® Si-e surgical system (Intuitive Surgical, Sunnyvale, CA, USA) and the subsequent 6 consecutive patients who had TaTME using the transanal endoscopic operation (TEO) device (Karl Storz Endoscopy, Tuttlingen, Germany) for low rectal cancers were included. All 27 surgeries were performed by a single experienced laparoscopic surgeon (FC Seow) from August 2012 to June 2015. Patients who had low or high anterior resections were excluded. Information was collected retrospectively. Statistical analysis was performed using SPSS version 21 (SPSS, Chicago, IL, USA). Mann-Whitney U test was used for the analysis of non-parametric continuous variables while Fisher's exact test was performed for analysis of categorical data. $P < 0.05$ was taken as significant.

All 21 RTMEs were performed using the 3-armed da Vinci Si-e surgical system. All patients underwent a hybrid technique consisting of an initial laparoscopic vascular ligation and left colonic mobilisation. The patient cart was docked and the rectum was completely mobilised to the anorectal junction. The anorectal junction was then transected using a linear stapler. The bowel was exteriorised via the umbilical camera port site and the appropriate part of the colon was removed. A 3 cm to 5 cm colonic J-pouch was then fashioned. Anastomosis with the remnant anal canal was performed laparoscopically with a transanal circular stapler, after reinsufflation of the peritoneal cavity. A defunctioning ileostomy was created in all patients.

Six patients underwent the taTME procedure. The first phase of this procedure was the laparoscopic management of the inferior mesenteric vessels and left colon. In the perineal phase, the Karl Storz TEO rectoscope was fixed in place with the insufflation pressure set to 12 mmHg with an airflow of 6 L/min. A purse-string was inserted at a distance below the lower edge of the tumour. A circumferential full thickness incision was made below the level of the purse-string. The dissection proceeded to the top of the levator plate and outwards to the pelvic side wall circumferentially to meet the laparoscopic plane. The fully mobilised colon and rectum were then prolapsed through the anal sphincters and amputated. A colonic J-pouch was then created and returned to the pelvis with a long string attached to the inserted stapler anvil for retrieval. A purse-string suture was applied to the distal anal stump, following which, the TEO rectoscope was removed. The J-pouch was pulled down. The distal anal purse-string was tightened securely around the shaft of the anvil and anastomosis was secured. The colonic pouch orientation was checked laparoscopically prior to stapler firing. A right iliac fossa defunctioning ileostomy was then created.

Results

Surgical parameters between the 2 groups are summarised in Table 1. There was no difference between the groups in terms of gender, body mass index (BMI), use of preoperative chemoradiotherapy, tumour size or distance of the inferior edge of the tumour from the anal verge. All resected TME specimens were examined by an experienced histopathologist, with all but 1 being described as complete. Proximal, distal and radial margin lengths were similar in both groups. There was no significant difference in operative duration or length of hospital stay. One patient in the RTME group with locally advanced disease required conversion to open surgery. Of the 3 patients in the RTME group with local recurrence, 2 had locally advanced pelvic nodal disease and 1 had distant metastases at the time of resection. No patient from either group suffered intraoperative or postoperative complications, and none died within the first 30 days post-surgery.

Table 1. Patient, Disease and Surgery Characteristics

	RTME	taTME	*P* Value
	Proportion (%)/Median (IQR)		
Number of patients	21	6	
Male	14 (67%)	3 (50%)	0.387
BMI	24 (22 – 26)	24 (20 – 27)	0.932
Neoadjuvant CRT	7 (33%)	2 (33%)	0.695
TNM Stage			
I	3 (14%)	0	
II	6 (29%)	2 (33%)	
III	9 (43%)	2 (33%)	
IV	3 (14%)	2 (33%)	
Differentiation			
Well	1 (5%)	2 (33%)	
Moderately	15 (71%)	2 (33%)	
Mucinous	5 (24%)	2 (33%)	
Distance from anal verge (mm)	50 (45 – 85)	70 (55 – 80)	0.662
Tumour size (mm)	35 (21 – 48)	39 (23 – 61)	0.357
Duration of surgery (minutes)	120 (100 – 200)	125 (99 – 135)	0.629
Proximal margin (mm)	70 (60 – 140)	85 (54 – 106)	0.977
Distal margin (mm)	12 (5.0 – 20)	12 (2.0 – 15)	0.512
Radial margin (mm)	5.0 (3.0 – 8.5)	2.3 (1.8 – 21)	0.476
Number of nodes harvested	16 (11 – 22)	13 (4.8 – 52)	0.842
Length of stay (days)	4 (3 – 5)	4 (3 – 7)	0.932
Length of follow-up (months)	28 (22 – 38)	30 (29 – 35)	0.589
Local recurrence	3 (14%)	0	

BMI: Body mass index; CRT: Chemoradiotherapy; IQR: Interquartile range; RTME: Robotic total mesorectal excision; taTME: Transanal total mesorectal excision; TNM: TNM classification of malignant tumours

Discussion

Three recent papers showed that robotic surgery compared to laparoscopic surgery for rectal cancer had a lower conversion rate, with similar overall postoperative morbidity and short-term oncological outcomes.[1-3] This may be taken to mean that robotic surgery has surgical advantages over laparoscopic surgery. Nonetheless, even with robotic technology, ensuring adequate distal and circumferential margins in anatomically unfavourable tumours may not be straightforward.

taTME is logically very attractive. The distal margin may be logically secured before rectal transection, guaranteeing clearance at the start of surgery in taTME. Dissection of the anorectum can also proceed regardless of pelvic narrowness and fat, which would otherwise make conventional laparoscopic or robotic surgery difficult. Recent results from the international taTME registry of 720 patients showed an 85% intact TME specimen rate, a 6.3% abdominal conversion rate from laparoscopic to open or transanal, and a 2.8% perineal conversion rate to a more extensive abdominal dissection.[4] Various recent studies have demonstrated similar postoperative complication rates, pathological and short-term oncological outcomes of taTME compared with laparoscopic TME.[5-8] A 2016 meta-analysis showed that taTME resulted in a larger CRM distance with lower risks of CRM positivity, higher rates of complete TME and a shorter operative duration compared with laparoscopic surgery.[9]

Conclusion

In this study, there was no significant difference in the length of the margins obtained; in particular, distal margins in both groups were similar. Nevertheless, we found it subjectively easier to secure and be confident of the lateral and distal margins for difficult low rectal cancers during RTME and TaTME compared to our prior experience with laparoscopic TME. Other authors have also shown this to be so.[10] As minimally invasive colorectal surgery becomes more widely available, surgeons should not be fixated on any one kind of technique. Instead, adequate training in all modalities of surgery may help combine the advantages of each to produce the best outcome for the patient.

REFERENCES

1. Mak TW, Lee JF, Futaba K, Hon SS, Ngo DK, Ng SS. Robotic surgery for rectal cancer: a systematic review of current practice. World J Gastrointest Oncol 2014;6:184-93.
2. Staderini F, Foppa C, Minuzzo A, Badii B, Qirici E, Trallori G, et al. Robotic rectal surgery: state of the art. World J Gastrointest Oncol 2016;8:757-71.
3. Biffi R, Luca F, Bianchi PP, Cenciarelli S, Petz W, Monsellato I, et al. Dealing with robot-assisted surgery for rectal cancer: current status and perspectives. World J Gastroenterol 2016;22:546-56.
4. Penna M, Hompes R, Arnold S, Wynn G, Austin R, Warusavitarne J, et al; TaTME Registry Collaborative. Transanal total mesorectal excision: international registry results of the first 720 cases. Ann Surg 2017;266:111-7.
5. Chen CC, Lai YL, Jiang JK, Chu CH, Huang IP, Chen WS, et al. Transanal total mesorectal excision versus laparoscopic surgery for rectal cancer receiving neoadjuvant chemoradiation: a matched case-control study. Ann Surg Oncol 2016;23:1169-76.
6. Marks JH, Montenegro GA, Salem JF, Shields MV, Marks GJ. Transanal TATA/TME: a case-matched study of taTME versus laparoscopic TME surgery for rectal cancer. Tech Coloproctol 2016; 20:467-73.
7. Rasulov AO, Mamedli ZZ, Gordeyev SS, Kozlov NA, Dzhumabaev HE. Short-term outcomes after transanal and laparoscopic total mesorectal excision for rectal cancer. Tech Coloproctol 2016;20:227-34.

8. Ma B, Gao P, Song Y, Zhang C, Zhang C, Wang L, et al. Transanal total mesorectal excision (taTME) for rectal cancer: a systematic review and meta-analysis of oncological and perioperative outcomes compared with laparoscopic total mesorectal excision. BMC Cancer 2016;16:380.
9. Xu W, Xu Z, Cheng H, Ying J, Cheng F, Xu W, et al. Comparison of short-term clinical outcomes between transanal and laparoscopic total mesorectal excision for the treatment of mid and low rectal cancer: a meta-analysis. Eur J Surg Oncol 2016;42:1841-50.
10. Deijen CL, Velthuis S, Tsai A, Mavroveli S, de Lange-de Klerk ES, Sietses C, et al. COLOR III: a multicentre randomised clinical trial comparing transanal TME versus laparoscopic TME for mid and low rectal cancer. Surg Endosc 2016;30:3210-5.

Isaac Seow-En, [1]*MBBS, MMed (Surgery), MRCSEd*, Francis Seow-Choen, [2]*MBBS, FRCSEd, FAMS*

[1]Department of Colorectal Surgery, Singapore General Hospital, Singapore
[2]Seow-Choen Colorectal Centre, Singapore

Address for Correspondence: Dr Francis Seow-Choen, Seow-Choen Colorectal Centre, 290 Orchard Road, #06-06 Paragon Shopping Centre, Singapore 238859.
Email: seowchoen@colorectalcentre.com

Neuroimaging in Juvenile Alexander Disease: Tumour-like Brainstem Lesions

Dear Editor,

Alexander disease (AD) is a progressive degenerative leukodystrophy, which typically presents in infancy. Neonatal, juvenile and adult-onset forms of AD are relatively rare, with a more variable clinical course compared to the infantile subtype. This disorder is a consequent of de novo heterozygous missense mutations in the *glial fibrillary acidic protein (GFAP)* gene. Characteristic imaging findings in AD have been described in the literature and are primarily supratentorial in distribution, with a frontal predominance. We describe 2 cases of genetically confirmed juvenile-onset AD, presenting as focal tumour-like lesions within the brainstem. Magnetic resonance imaging (MRI) characteristics of these lesions are discussed, along with clues to differentiate this entity from other focal brainstem lesions within the paediatric population (such as focal glioma and demyelinating lesion). These cases highlight an atypical presentation of juvenile AD and the need for consideration of metabolic diseases when focal tumour-like brainstem lesions are encountered, thus allowing an accurate diagnosis and avoiding invasive investigation by means of tissue biopsy.

Case 1

A 7-year-old boy was referred to our neuro-oncology unit for a presumed tumour within the dorsal medulla oblongata. The child had a longstanding history of motor developmental delay, congenital hip dysplasia and progressive weakness of the lower limbs. At the time of referral, no definitive cause for his symptoms had been found. One year prior to presentation, he developed intractable vomiting resulting in emaciation. MRI of the brain demonstrated a well circumscribed symmetrical lesion in the dorsal medulla (Figs. 1A-E), concerning for a brainstem glioma. The case was presented at the neuro-oncology meeting for consideration of biopsy or initiation of proton beam therapy. However, the unusually symmetric appearance of the lesion prompted the consideration of atypical AD. Mutation analysis of the *GFAP* gene revealed a pathogenic *GFAP* gene mutation (heterozygous C>T nucleotide substitution in exon 4 at amino acid position 258), confirming the diagnosis of AD.

Case 2

A 14-year-old girl was referred to the local paediatric services for failure-to-thrive and learning difficulties. This was associated with persistent vomiting and severe weight loss. No motor symptoms were present at the time of presentation. Neurological examination was unremarkable apart from slight brisk reflexes in the lower limbs. MRI of the brain showed a well defined, bilobulated, enhancing lesion within the dorsal medulla on a background of leukodystrophy with some cystic elements and mild frontal predominance. The lesion within the dorsal medulla was not present in a MRI study done 5 years prior to current presentation for investigation of developmental delay (Figs. 1F-I). The overall imaging appearances were suggestive of juvenile AD. Sequencing of *GFAP* revealed a mutation in exon 1: c.262C>T: p.Arg88Cys, confirming the diagnosis of juvenile AD. Three years later, the patient presented to the emergency department for dense right hemiplegia and hemineglect after prolonged seizure. Repeat MRI of the brain showed progression of leukodystrophy as well as a new area of signal abnormality within the left cerebral hemisphere, involving predominantly the cortical grey matter. The lesion in the dorsal medulla showed interval regression. There was heterogenous signal abnormality within the atrophic medulla. Extensive neuro-metabolic and neuro-inflammatory investigations were performed but yielded no significant abnormality. The case was discussed at the neurology meeting and it was felt that the patient's new onset right hemiplegia was likely due to evolution of her genetically confirmed AD.

Discussion

AD is a progressive degenerative leukodystrophy associated with the presence of Rosenthal fibres on histology and dominant mutations in the *GFAP* gene on chromosome 17q21.[1,2] Rosenthal fibres are eosinophilic inclusion bodies found in astrocytes that contain *GFAP*, ubiquitin as well as small stress proteins αβ-crystalline and heat shock protein.[3,4] Neonatal, infantile, juvenile and adult forms of AD have been described.[5] In 2011, Prust et al proposed a revision of the subtypes of AD into 2 major groups—Type 1 and Type II. Type 1 AD is characterised by early onset and typical MRI features. Type II, on the other hand, is characterised by later onset, bulbar symptoms and atypical MRI features,[6] as illustrated in both cases.

AD presenting as an isolated lesion within the brainstem is rare. To our knowledge, only 3 cases of juvenile AD

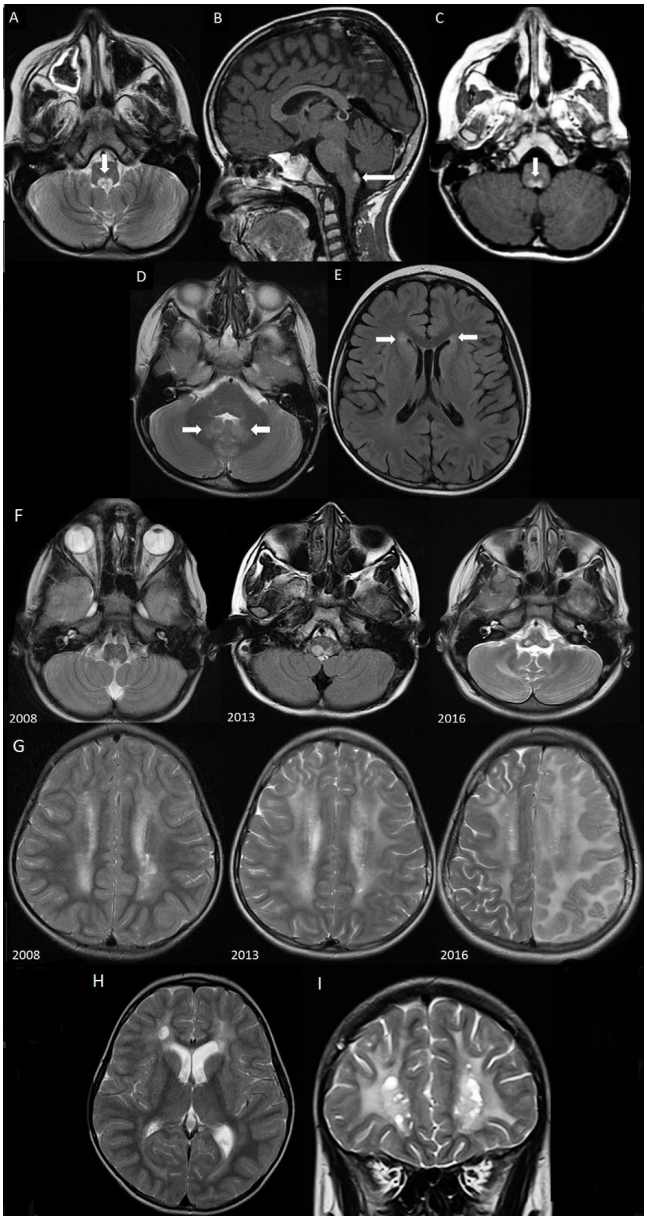

Fig. 1. Patient 1: Axial T2-weighted image (A) demonstrates a well circumscribed, hyperintense and symmetrical lesion in the dorsal medulla oblongata with minimal mass effect. Sagittal (B) and axial (C) postcontrast images show avid homogeneous enhancement of the prior described lesion within the dorsal medulla. Ill-defined non-enhancing signal abnormality is also seen in the dentate nuclei (D) and frontal periventricular white matter (E). Patient 2: Serial MRI studies were performed from 2008 to 2016, illustrating the progression of imaging findings. (F) Serial axial T2-weighted images show a well defined, bi-lobulated enhancing lesion within the dorsal medulla, first seen in 2013 and subsequently underwent regression in 2016, associated with atrophy of the medulla. (G) Serial axial T2-weighted images showed temporal progression of the leukodystrophy. In 2016, new diffuse signal abnormality is seen within the left cerebral hemisphere, involving predominantly the cortical grey matter. This was presumed to be an atypical pattern of disease progression. Axial (H) and coronal (I) T2-weighted images demonstrate cystic changes within the frontal lobes.

presenting in this manner have been reported in the English literature. The described cases add to the existing literature that neurodegenerative disease should be considered in the differential diagnosis for focal tumour-like brainstem lesions. The other considerations for such lesions include focal tumours, typically gliomas in this age group, infections and demyelinating disorders.[7] In 2001, van der Knaap et al proposed a MRI-based imaging criteria for establishing the diagnosis of AD.[5,8] Over the years, the clinical and MRI phenotypic variations in AD have been increasingly recognised. In a 2005 study by van der Knaap et al,[10] patients with clinical features suggestive of AD who did not meet the typical diagnostic MRI criteria were found to have *GFAP* missense mutations on genetic analysis. Atypical MRI features found in these patients include predominant or isolated involvement of posterior fossa structures (as seen in Case 1), multifocal tumour-like brainstem lesions and brainstem atrophy, diffuse signal changes involving the deep grey nuclei, garland-like feature along the ventricular wall and characteristic pattern of contrast enhancement.[9] In both of our cases, the brainstem lesions were confined to the dorsal medulla oblongata. The brainstem lesions associated with juvenile AD tend to demonstrate avid homogenous contrast enhancement,[9,10,11] as seen in both of our cases. In AD dominated by brainstem and spinal abnormalities, medulla involvement is invariably present.[9]

The differentiation of tumour-like brainstem lesions of AD from gliomas and demyelinating disease is crucial as the treatment varies tremendously. Gliomas are the most common brainstem neoplasm in children, accounting for approximately 90% of the cases.[12,13] The absence of enhancement is an extremely useful imaging feature in differentiating this entity from brainstem lesions of AD, which usually shows homogenous enhancement. Unfortunately, although the absence of enhancement is the norm, there are exceptions to the rule.[14] Enhancement in gliomas and demyelinating disease (if present) is usually ring-like or spotty.

Demyelinating disease is another mimic of brainstem lesions of AD. Differentiation of these 2 conditions based solely on imaging is a radiological challenge. Correlation with patient's age, clinical features and results of other investigations is mandatory. Multiple sclerosis (MS) is rare in children. MS lesions in the brainstem tend to be sited along the floor of the 4th ventricle and on the surface of the pons.[15] Demonstration of typical supratentorial MS lesions (when present) may assist the reporting radiologist in reaching the correct diagnosis. Additional lesions should also be sought within the rest of the spinal cord as acute demyelinating encephalomyelitis (ADEM) rarely presents in the form of a solitary brainstem lesion without evidence of more disseminated intracranial involvement. The

clinical presentation also differs substantially and includes encephalopathy. The medulla oblongata is the most common site of involvement in neuromyelitis optica (NMO). Lesions of NMO usually show an ill defined margin, compared to those of AD. In addition, detection of blood antibody NMO-immunoglobulin (IgG) has been reported to have a 90% specificity rate and hence can be extremely useful to exclude the diagnosis of NMO.[16]

As high as 98% of AD cases are associated with mutations in the coding region of the *GFAP* gene.[17,18] The availability of molecular genetic testing has opened new directions for investigation. These cases highlight an atypical presentation of juvenile AD and the need for consideration of metabolic diseases when focal tumour-like brainstem lesions are encountered. This is to ensure that the appropriate investigations such as genetic testing are conducted, bypassing the need for invasive investigation such as brainstem biopsy which carries significant morbidity.

REFERENCES

1. Li R, Johnson AB, Salomons G, Goldman JE, Naidu S, Quinlan R, et. al. Glial fibrillary acidic protein mutation in infantile, juvenile and adult forms of Alexander Disease. Ann Neurol 2005;57:310-26.
2. Li R, Messing A, Goldman JE, Brenner M. GFAP mutations in Alexander disease. Int J Dev Neurosci 2002;20:259-68.
3. Brenner M, Johnson AB, Boespflug-Tanguy O, Rodriguez D, Goldman JE, Messing A. Mutations in GFAP, encoding glial fibrillary acidic protein are associated with Alexander disease. Nat Genet 2001;27:117-20.
4. Johnson A. Alexander disease: a review and the gene. Int J Dev Neurosci 2002;20:391-4.
5. van der Knaap MS, Naidu S, Breiter SN, Blaser S, Stroink H, Springer S, et al. Alexander disease: diagnosis with MR imaging. AJNR Am J Neuroradiol 2001;22:541-52.
6. Prust M, Wang J, Morizono H, Messing A, Brenner M, Gordon E, et al. GFAP mutations, age at onset and clinical subtypes in Alexander disease. Neurology 2011;77:1287-94.
7. Guzman-De-Villora JA, Fernandez-Garcia P, Ferreiro-Arguelles C. Differential diagnosis of T2 hyperintense brainstem lesions: part 1. Focal lesions. Semin Ultrasound CT MR 2010;31:246-59.
8. Rodriguez D, Gauthier F, Bertini E, Bugiani M, Brenner M, N'guyen S, et al. Infantile Alexander disease: spectrum of GFAP mutations and genotype-phenotype correlation. Am J Hum Genet 2001;69:1134-40.
9. van der Knaap MS, Salomons GS, Li R, Franzoni E, Gutiérrez-Solana LG, Smit LM, et al. Unusual variants of Alexander's disease. Ann Neurol 2005;57:327-38.
10. van Poppel K, Broniscer A, Patay Z, Morris EB. Alexander disease: an important mimicker of focal brainstem glioma. Pediatr Blood Cancer 2009;53:1355-6.
11. Franzoni E, van der Knaap MS, Errani A, Colonnelli MC, Bracceschi R, Malaspina E, et al. Unusual diagnosis in a child suffering from juvenile Alexander disease: clinical and imaging report. J Child Neurol 2006;21:1075-80.
12. Kwon JW, Kim IO, Cheon JE, Kim WS, Moon SG, Kim TJ, et al. Paediatric brain-stem gliomas: MRI, FDG-PET and histological grading correlation. Pediatr Radiol 2006;36:959-64.
13. Guillamo JS, Doz F, Delattre JY. Brain stem gliomas. Curr Opin Neurol 2001;14:711-5.
14. Vandertop WP, Hoffman HJ, Drake JM, Humphreys RP, Rutka JT, Amstrong DC, et al. Focal midbrain tumors in children. Neurosurgery 1992;31:186-94.
15. Yousry TA, Grossman RI, Filippi M. Assessment of posterior fossa damage in MS using MRI. J Neurol Sci 2000;172:S50-3.
16. Park KY, Ahn JY, Cho JH, Choi YC, Lee KS. Neuromyelitis optica with brainstem lesion mistaken for brainstem glioma. Case report. J Neurosurg 2007;107:251-4.
17. Gordon N. Alexander disease. Eur J Paediatr Neurol 2003;7:395-9.
18. Ferreira MC, Dorboz I, Rodriguez D, Boespflug Tanguy O. Screening for GFAP rearrangement in a cohort of Alexander disease and undetermined leukoencephalopathy patients. Eur J Med Genet 2015;58:466-70.

Ai Peng Tan, [1]*MD*, Chhabda Sahil,[2]*MBBS*, Robert Robinson,[3]*MBBS*, Ata Siddiqui, [4]*MD*, Elizabeth Wraige, [5]*MD*, Christopher Chandler, [6]*MBBS*, Kshitij Mankad,[3]*MBBS*

[1]Department of Diagnostic Imaging, National University Hospital, National University Health System, Singapore
[2]Department of Radiology, Chelsea and Westminster Hospital, NHS Foundation Trust, United Kingdom
[3]Department of Neurology, Great Ormond Street Hospital, NHS Foundation Trust, United Kingdom
[4]Department of Radiology, Guy's and St Thomas', NHS Foundation Trust, United Kingdom
[5]Department of Neurology, Guy's and St Thomas', NHS Foundation Trust, United Kingdom
[6]Department of Neurosurgery, King's College Hospital, NHS Foundation Trust, United Kingdom

Address for Correspondence: Dr Tan Ai Peng, Department of Diagnostic Imaging, National University Hospital, National University Health System, 1E Kent Ridge Road, Singapore 119228.
Email: ai_peng_tan@nuhs.edu.sg

Letter to the Editor

A Case Note on Legionnaires' Disease Caused by Serogroup 1, Sequence Type ST496 in Singapore

Dear Editor,

Legionella pneumophila has previously been found to be endemic in Singapore.[1-3] Local environmental isolates have been studied and characterised,[2-4] but speciation of local clinical isolates from patients with Legionnaires' disease has, to our knowledge, not been reported. As a result, the link between environmental and disease-causing *Legionella* isolates in Singapore remains elusive. Herein, we described a case of Legionnaires' disease in Singapore, and the serogroup, allelic profile and sequence type of the clinical isolates recovered.

A 61-year-old local Chinese male was admitted to the intensive care unit (ICU) of Ng Teng Fong General Hospital for acute hypoxemic respiratory failure. He was a shipboard repair engineer, and had comorbidities of ischaemic heart disease, hypertension, dyslipidaemia and chronic obstructive pulmonary disease. He had first developed symptoms of acute breathlessness, productive cough and fever while at sea, and was initially treated by a shipboard physician with a course of oral antibiotics.

The patient lived in a naturally ventilated apartment equipped with an instantaneous water heater system—there was no hot water storage tank. He stayed aboard cruise ships for work a few days each time. He did not repair pipes or water tanks. His family and colleagues were reported to be well.

The patient subsequently presented to our hospital upon disembarkation after 3 days of illness as his condition had deteriorated. He was dyspnoeic and septic on admission. Clinical examination revealed absence of breath sounds over the left lung base. The blood pressure was 93/60 mmHg, pulse was 110 beats per minute, temperature was 38.7°C, respiratory rate was 26 breaths per minute and peripheral oxygen saturation (SpO_2) was 84% on room air and 95% on non-rebreather mask. A chest radiograph revealed dense left lower zone consolidation with air bronchogram, and a diagnosis of severe pneumonia was made. Intravenous amoxicillin-clavulanate, ceftazidime and azithromycin therapy was initiated as per hospital guidelines for severe community-acquired pneumonia, and the patient was admitted to the ICU.

Investigations revealed leucocytosis of 13.95 x 109/L (reference range: 3.37-11.03 x 109/L), serum creatinine of 155 μmol/L (reference range: 64-104 μmol/L), serum lactate of 1.0 mmol/L (reference range: 0.0-1.8 mmol/L), and type 1 respiratory failure on arterial blood gas (PaO_2 71.8 mmHg, $PaCO_2$ 32.3 mmHg, FiO_2 of 1.00). The patient was intubated, and treated with bronchodilators, intravenous steroid, and paralysis for severe bronchospasm.

Urine *Legionella* antigen testing (Alere BinaxNOW *Legionella* urinary antigen card) returned positive on the second day of hospitalisation. Antibiotics were rationalised to a week of azithromycin monotherapy. The patient improved rapidly thereafter, was successfully extubated on the third day, and was discharged after 7 days of hospitalisation.

Two endotracheal tube (ETT) aspirate samples were obtained and sent to the Environmental Health Institute's laboratory for isolation of *Legionella pneumophila*, and for sequence-based typing.[4,5] Both samples were directly plated on glycine, vancomycin, polymyxin B, cicloheximide (GVPC) and buffered charcoal yeast extract, alpha-ketoglutarate containing L-cysteine (L-cysteine-BCYEα) agars (Oxoid, Thermo Fisher Scientific), and incubated at 36 ± 1ºC for up to 10 days. The plates were observed daily and colonies were observed 3 days after inoculation. Purified polymerase chain reaction (PCR) products were sequenced by capillary electrophoresis using Applied Biosystems® 3730/3730xl deoxyribonucleic acid (DNA) Analyzer and BigDye Terminator v3.1 (Axil Scientific, Singapore). Latex agglutination test (*Legionella* latex test, Oxoid) revealed that the *L. pneumophila* isolates from the 2 endotracheal aspirates samples belonged to serogroup 1, and sequencing identified them as belonging to sequence type (ST) 496.

L. pneumophila serogroup 1 (Lp1) has been reported to be the most common (61-88%) serogroup responsible for Legionnaires' disease.[6,7] In this case study, we successfully used sequence-based typing—the gold standard method for subtyping *L. pneumophila*—to characterise and sequence type local clinical Lp1 isolates to ST496. ST496 was previously isolated from clinical samples in the Netherlands (2003) and environmental sampling of spa pools in Singapore (2006).[4,8] Our findings demonstrate that ST496 is also associated with sporadic human cases in Singapore.

In Singapore, suspected cases of Legionnaires' disease are usually tested only with urinary antigen test specific for Lp1, without further attempts to isolate *L. pneumophila*.[2,9]

Thus, the diversity of *L. pneumophila* strains among the Lp1 population is not characterised, preventing comparison of clinical and environmental isolates for outbreak investigations and epidemiological research by public health professionals. Sequence typing of these clinical isolates has provided additional information on the genetic profile of local Lp1 strains, which would ultimately facilitate better understanding of the local molecular epidemiology and ecology of *L. pneumophila*. Our study highlights the importance of obtaining microbiological culture and isolation of *L. pneumophila* (besides urinary antigen testing) in suspected clinical cases so as to aid matching with environmental and other clinical isolates in the future.

Acknowledgements

The authors would like to thank the following: Associate Professor Ng Lee Ching (Director of the Environmental Health Institute; Adjunct Associate Professor, School of Biological Science, Nanyang Technological University) for her support of this study and proof-reading the manuscript; Ms Lalitha Kurupatham (Senior Assistant Director of Policy & Control Branch, Communicable Diseases Division; Head, National Public Health Unit) for notifying the Environmental Health Institute (National Environmental Agency) of this case; and Dr Nitin Mahobia (Consultant Microbiologist, Department of Laboratory Medicine, Ng Teng Fong General Hospital) for facilitating the collection of specimens for testing at the Environmental Health Institute laboratory.

REFERENCES

1. Lam MC, Ang LW, Tan AL, James L, Goh KT. Epidemiology and controlof Legionellosis, Singapore. Emerg Infect Dis 2011;17:1209-15.
2. Goh KT, Ng DLK, Yap J, Ma S, Ooi EE. Surveillance, prevention, and control of legionellosis in a tropical city-state. Am J Infect Control 2005;33:286-91.
3. Heng BH, Goh KT, Ng DL, Ling AE. Surveillance of legionellosis and Legionella bacteria in the built environment in Singapore. Ann Acad Med Singapore 1997;26:557-65.
4. Lim YH, Relus Kek YL, Lim PY, Yap HM, Vivien Goh TL, Ng LC. Environmental surveillance and molecular characterization of Legionella in tropical Singapore. Trop Biomed 2011;28:149-59.
5. Gaia V, Fry NK, Afshar B, Lück PC, Meugnier H, Etienne J, et al. Consensus sequence-based scheme for epidemiological typing of clinical and environmental isolates of Legionella pneumophila. J Clin Microbiol 2005;43:2047-52.
6. Reimer AR, Au S, Schindle S, Bernard KA. Legionella pneumophila monoclonal antibody subgroups and DNA sequence types isolated in Canada between 1981 and 2009: laboratory component of national surveillance. Eur J Clin Microbiol Infect Dis 2010;29:191-205.
7. Tijet N, Tang P, Romilowych M, Duncan C, Ng V, Fisman DN, et al. New endemic Legionella pneumophila serogroup I clones, Ontario, Canada. Emerg Infect Dis 2010;16:447-54.
8. The European Working Group for Legionella Infections. Legionella pneumophila sequence-based typing. Available at: http://bioinformatics.phe.org.uk/legionella/legionella_sbt/php/sbt_homepage.php. Accessed on 6 March 2017.
9. Cunha BA, Burillo A, Bouza E. Legionnaires' disease. Lancet 2016;387:376-85.

Leyland Chuang, [1]*MBBS, MRCP*, Kyaw Thu Aung,[2]*MBBS, MSc, PGDip*, Joanne SL Kang, [3]*PhD*, Merrill Lim, [4]*Dip (Information Technology)*, Charlene Kang, [4]*MSc*, Ramona Alikiiteaga Gutiérrez, [5]*DVM, PhD*, Jennifer HM Yap,[4]*MSc*

[1]Department of Medicine, Ng Teng Fong General Hospital, Singapore
[2]Food Hygiene Risk Assessment & Mitigation Group, Environmental Health Institute, National Environment Agency, Singapore
[3]Food Microbiology, Environmental Health Institute, National Environment Agency, Singapore
[4]Environmental Hygiene Investigation Group, Environmental Health Institute, National Environment Agency, Singapore
[5]Food and Environmental Hygiene Research Programme, Environmental Health Institute, National Environment Agency, Singapore

Address for Correspondence: Ms Jennifer Yap Hooi Ming, Environmental Hygiene Investigation Group, Environmental Health Institute, National Environment Agency, #06-05/08, Helios Block, 11 Biopolis Way, Singapore 138667.
Email: Jennifer_yap@nea.gov.sg

The Effectiveness of a Pharmacist-Led Sun Protection Counselling Service: Results from a Tertiary Dermatology Centre in Singapore

Dear Editor,

Exposure to ultraviolet (UV) radiation is associated with an increased risk of skin cancer, and the incidence of skin cancer is increasing worldwide. Sun exposure also aggravates other dermatological conditions such as rosacea.

Awareness of the importance of sun protection and sun protection behaviour patterns varies greatly amongst individuals. Young children are mostly guided by their parents,[1] while adolescents tend to have the lowest sun protection rates and are largely influenced by the entertainment industry and social media.[2-4] Adult women are more likely than men to take sun protective measures.[3,5-6]

A number of studies has demonstrated that sun protection counselling by healthcare providers can have positive effects on knowledge and prevention practices.[7-8] However, most of these studies have been carried out in Caucasians and the paediatric population.[1,7-9] In addition, previous data has showed that in general, few physicians provide sun protection education—the biggest obstacles cited include lack of proper training and insufficient time.[10-11] Several papers have reported that there is a role for pharmacists in educating patients about sun protection.[12-14]

Therefore, the aim of this study was to assess and compare sun protection-related knowledge and behaviours within a group of patients and non-medical staff members at a tertiary dermatology centre in Singapore, and to evaluate the effectiveness of a dedicated pharmacist-led counselling service in improving understanding.

Materials and Methods

Our study was conducted from May to October 2013. Fifty patients who were on follow-up at the National Skin Centre (NSC) and 50 non-medical staff members (nurses, pharmacy technicians, clinic assistants and administrative staff) were recruited. The patients included those who were deemed by their attending physician to require sun protection counselling, as well as patients who agreed to be included in the study.

Demographic characteristics and details regarding each subject's usual sun protection behaviours were gathered. The participants answered a 10-question questionnaire designed by the authors to assess sun protection understanding, attitudes and behaviours (Appendix). Each subject then underwent a standardised 20-minute counselling session with the aid of a computer slide presentation by a trained pharmacist. The participants were surveyed again immediately after the session to assess the efficacy of the intervention.

Results

Baseline Characteristics of Study Subjects

These are detailed in Table 1. The mean age was higher in the patient group (47.9 years compared to 34.1 years). The 50 patients consisted of an equal number of males and females, while most of the 50 staff members were female (37/50 or 74%). Most of our study subjects had black hair

Table 1. Characteristics of Study Subjects

Characteristic	Patients (n = 50)	Staff Members (n = 50)
Age (years)	13 – 89	23 – 64
Mean	47.9	34.1
Gender		
Male	25	13
Female	25	37
Hair colour		
Black	37	43
Brown	12	7
Blonde	1	
Skin colour		
Very fair	2	
Fair	19	22
Light brown	21	22
Dark brown	7	6
Data unavailable	1	
Fitzpatrick skin type		
I	3	1
II	15	5
III	14	20
IV	7	11
V	4	4
VI	6	1
Data unavailable	1	

Table 1. Characteristics of Study Subjects (Cont'd)

Characteristic	Patients (n = 50)	Staff Members (n = 50)
Education level		
Primary	2	
Secondary	16	12
Pre-university	13	13
University	4	13
Postgraduate	14	10
Data unavailable	1	2
Occupation		
Indoor	31	50
Outdoor	6	
Indoor and outdoor	5	
Retired	6	
Data unavailable	2	
Hours spent in the sun per week	0.5 – 42.5	1 – 36
Mean	8.72	6.76
No. of sunburns in the past 1 year	0 – 8	0 – 6
Mean	0.67	0.94
Family history of skin cancer		
Yes	3	2
No	47	48

Table 2. Baseline Sun Protection Behaviours

Behaviour	Patients n = 50 (%)	Staff Members n = 50 (%)
Daily sunscreen use		
Regular	15 (30)	21 (42)
Occasional	13 (26)	14 (28)
Never	22 (44)	15 (30)
Use of hat when outdoors		
Yes	12 (24)	2 (4)
No	37 (74)	43 (86)
Data unavailable	1 (2)	5 (10)
Use of umbrella when outdoors		
Yes	9 (18)	14 (28)
No	40 (80)	33 (66)
Data unavailable	1 (2)	3 (6)
Wearing protective clothing when outdoors		
Yes	25 (50)	17 (34)
No	24 (48)	28 (56)
Data unavailable	1 (2)	5 (10)
Staying out of the sun as far as possible		
Yes	43 (86)	41 (82)
No	7 (14)	6 (12)
Data unavailable		3 (6)

(80/100 or 80%) and light brown skin (43/99 or 43.4%), and were of Fitzpatrick skin types II/III/IV (72/98 or 73.5%). There were more staff members who had university and postgraduate qualifications (47.9% compared to 36.7%). On average, patients spent more time outdoors per week (8.72 hours compared to 6.76 hours). Notably, however, staff members sustained more sunburns over the past 1 year (0.94 burns compared to 0.67 burns). Three patients and 2 staff members reported a family history of skin cancer.

Baseline Sun Protection Behaviours

These are described in Table 2. Only one-third of the patients and less than half (42%) of the staff cohort applied sunscreen daily. Out of the 63 study subjects who used sunscreen, 42 or 66.7% elected to use sunscreens that offered a sun protection factor (SPF) of more than 30 whilst 15 or 23.8% used sunscreens with a SPF of 30. Although 86% of the patients and 82% of the staff members tried to stay out of the sun as far as possible, the vast majority of our study population did not use hats (80/94 or 85.1%) or umbrellas (73/96 or 76.0%) when outdoors. Most of the subjects also did not wear protective clothing, such as long sleeves and pants (52/94 or 55.3%).

Pre-Counselling and Post-Counselling Results

Before counselling, the mean score was 4.66/10 amongst patients and 8.14/10 amongst staff. The majority of patients (11/50 or 22%) attained a score of 4/10, whilst most of the staff members (27/50 or 54%) achieved scores of 7/10 to 8/10.

After counselling, more patients and staff gave appropriate responses to each question in the questionnaire. The mean score was 6.88/10 in the patient group and 8.7/10 in the staff group. A higher proportion of patients (14/50 or 28%) and staff members (19/50 or 38%) scored full marks.

Discussion

To our knowledge, this is the first study to evaluate the efficacy of a pharmacist-led sun protection counselling service in Asia.

In general, there is a need to improve sun protection behaviours and educate individuals about proper sunscreen application. Although 43 out of 50 patients (86%) and all staff members were aware that sun exposure increases the risk of skin cancer pre-counselling, only a third of the patients and less than half (42%) of the staff cohort used sunscreen daily. The most common reasons given for not

using sunscreen were inconvenience and the perception that applying sunscreen was not important. Amongst the 63 subjects who used sunscreen, many (55/63 or 87.3%) did not reapply the sunscreen at all and about half (31/63 or 49.2%) applied it only to selected areas such as the face. In addition, the vast majority of our study population did not use hats or umbrellas when outdoors, nor did most of them wear protective clothing.

Previous data has shown that adolescents tend to have the lowest sun protection rates.[2-4] As we had only 2 adolescents amongst our study subjects, this precludes us from drawing any definitive conclusions. Nonetheless, we had a 13-year-old girl with vitiligo who reported only occasional use of sunscreen, with no sun avoidance behaviours. Although it has been noted that women are more likely to adhere to photoprotection than men,[3,5-6] our study yielded mixed results. Our female subjects were more likely to use sunscreen daily and use umbrellas when outdoors, but fewer wore hats or donned protective clothing.

Based on the total and mean scores, it was encouraging to note that the group of staff members as a whole had better knowledge and understanding compared to patients before counselling. It was also reassuring to see that the 3 patients who had a family history of skin cancer all registered higher scores than the average (8-10 versus an average score of 4.66). We had 2 patients with basal cell carcinoma, and they performed well with a mean score of 8.5. However, 20 patients with rosacea, vitiligo, photoaggravated eczema, sunburns, lentigenes, melasma and actinic keratoses had low scores ranging from 2.67 to 5.4. This is a worrying observation, and reflects the need to improve patient education.

Amongst both patients and staff, the 2 questions with the most wrong answers prior to counselling were "Clothing of lighter colour has more UV protection as it reflects sunlight – false" and "A sunscreen with SPF 30 provides twice the protection as a SPF 15 – false". It is important to correct these misconceptions.

After counselling, there was an improvement in sun protection knowledge and awareness. More patients and staff gave appropriate responses to each question. The mean scores also improved from 4.66 to 6.88 in the patient group, and from 8.14 to 8.7 in the staff cohort.

Language barriers hindered our counselling service at times. The pharmacists also experienced time constraints in the setting of a busy tertiary dermatology centre.

This study is limited by its small sample size, and the potential for recall and selection bias. Our study subjects are specific groups, and staff at a dermatology centre may be more familiar with sun protection. Although this impacts the applicability of our results, we feel that our results can serve as a guide. There was missing data, which was taken into account during analysis of our results. Despite our results showing better knowledge immediately post-counselling, individuals may not retain this level of understanding over time and this may not necessarily translate into improved photoprotection behaviours as well. It would be helpful to reassess the subjects again after a year to check for retention of knowledge.

Conclusion

In conclusion, the implementation of a specialised pharmacist-led sun protection counselling service is potentially useful in the education of patients. Larger studies need to be done in a more heterogeneous population, and we hope to use these results to promote the establishment of similar services in other dermatology centres worldwide.

Acknowledgements

The authors would like to thank the following National Skin Centre pharmacists for their invaluable contributions to the study by administering the questionnaires and performing sun protection counselling: Lee Foon Tang, Elizabeth Tian, Winnie Choo, Winnie Li, Germaine Chua, Weiyu Chen and Charles Tan.

REFERENCES

1. Cohen L, Brown J, Haukness H, Walsh L, Robinson JK. Sun protection counselling by pediatricians has little effect on parent and child sun protection behaviour. J Pediatr 2013;162:381-6.
2. Dobbinson S, Wakefield M, Hill D, Girgis A, Aitken JF, Beckmann K, et al. Prevalence and determinants of Australian adolescents' and adults' weekend sun protection and sunburn, summer 2003-2004. J Am Acad Dermatol 2008;59:602-14.
3. Eichhorn C, Seibold C, Loss J, Steinmann A, Nagel E. Knowledge about UV-radiation and sun protection: survey of adolescents and young adults in Bavaria. Hautarzt 2008;59:821-7.
4. Benvenuto-Andrade C, Cestari TF, Mota A, Poziomczyk C, Ramos-E-Silva M. Photoprotection in adolescence. Skinmed 2005;4:229-33.
5. Hall HI, May DS, Lew RA, Koh HK, Nadel M. Sun protection behaviours of the US white population. Prev Med 1997;26:401-7.
6. Miles A, Waller J, Hiom S, Swanston D. SunSmart? Skin cancer knowledge and preventive behaviour in a British population representative sample. Health Educ Res 2005;20:579-85.
7. Robinson JD, Silk KJ, Parrott RL, Steiner C, Morris SM, Honeycutt C. Healthcare providers' sun-protection promotion and at-risk clients' skin-cancer-prevention outcomes. Prev Med 2004;38:251-7.
8. Jung GW, Senthilselvan A, Salopek TG. Likelihood of dermatology patients to inquire about sun protection measures during a regular clinic visit. J Cutan Med Surg 2011;15:266-74.
9. Davy L, Boyett T, Weathers L, Campbell RJ, Roetzheim RG. Sun protection counselling by pediatricians. Ambul Pediatr 2002;2:207-11.

10. Cac NN, Walling HW, Vest C, Ting W. Differences in perceived importance and personal use of sun protection among primary care physicians are reflected in their clinical practice. Int J Dermatol 2008;47:137-43.
11. Geller AC, O'Riordan DL, Oliveria SA, Valvo S, Teich M, Halpern AC. Overcoming obstacles to skin cancer examinations and prevention counselling for high-risk patients: results of a national survey of primary care physicians. J Am Board Fam Pract 2004;17:416-23.
12. Souvignier ST, Mayer JA, Eckhardt L. Educating the public about skin cancer prevention: a role for pharmacists. J Clin Pharm Ther 1996:21:399-406.
13. Mayer JA, Eckhardt L, Stepanski BM, Sallis JF, Elder JP, Slymen DJ, et al. Promoting skin cancer prevention counselling by pharmacists. Am J Public Health 1998:88:1096-9.
14. Mayer JA, Slymen DJ, Eckhardt L, Rosenberg C, Stepanski BM, Creech L, et al. Skin cancer prevention counselling by pharmacists: specific outcomes of an intervention trial. Cancer Detect Prev 1998:22:367-75.

Shan Xian Lee, [1]*MBBS, MRCP (UK)*,
Wei Sheng Chong,[2]*MMed (Int Med), MRCP (UK), FRCP (Edin)*,
Xiu Ting Lauw,[2]*BSc(Pharm)(Hons)*,
Siew Kiang Tan, [3]*MBBS, MMed (Int Med), MRCP (UK)*,
Hazel H Oon, [2]*MD, MRCP (UK), FAMS*

[1]Department of Dermatology, Changi General Hospital, Singapore
[2]National Skin Centre, Singapore
[3]Raffles Medical Group, Raffles Hospital, Singapore

Address for Correspondence: Dr Lee Shan Xian, Department of Dermatology, Changi General Hospital, 2 Simei Street 3, Singapore 529889.
Email: shan_xian_lee@cgh.com.sg

Appendix

1. **Sun exposure increases the risk of skin cancer.**
   TRUE/FALSE/NOT SURE
2. **You can get skin cancer on non-sun exposed areas.**
   TRUE/FALSE/NOT SURE
3. **Sun exposure during childhood is related to skin cancer in adulthood.**
   TRUE/FALSE/NOT SURE
4. **You do not need to apply sunscreen if you stay indoors as window glass absorb rays.**
   TRUE/FALSE/NOT SURE
5. **You only need to take sun protective measures when the sun is at its highest pe the day.**
   TRUE/FALSE/NOT SURE
6. **You do not need to reapply sunscreen if you use sunscreen with the highest SPI**
   TRUE/FALSE/NOT SURE
7. **Clothing of lighter colour has more UV protection as the clothing reflects sunlig**
   TRUE/FALSE/NOT SURE
8. **You do not need to apply sunscreen if you use a moisturiser or makeup contain sunscreen.**
   TRUE/FALSE/NOT SURE
9. **A sunscreen with a SPF of 30 provides twice the protection as a SPF 15.**
   TRUE/FALSE/NOT SURE
10. **You do not need sun exposure at all as sun exposure brings no benefits.**
    TRUE/FALSE/NOT SURE

Letter to the Editor

Ethnic Differences in Preoperative Patient Characteristics and Postoperative Functional Outcomes after Total Knee Arthroplasty among Chinese, Malays and Indians

Dear Editor,

Osteoarthritis (OA) of the knee is a common condition and increases in occurrence and severity with advancing age.[1] Total knee arthroplasty (TKA) can significantly improve patient function and quality of life in cases of severe disease.[2-4]

However, preoperative and postoperative patient-reported outcomes may be influenced by physical characteristics—a well known example being body mass index (BMI).[5] In addition, ethnic differences in knee OA have been suggested in some large studies showing that African Americans in the general population had poorer preoperative functional scores, greater prevalence of valgus malalignment and greater severity of radiographic knee OA compared to Caucasians.[6-9] Joshy et al revealed that Indian and Pakistani patients had poorer preoperative Knee Society Scores compared to Caucasians in Birmingham, United Kingdom[10] while Gandhi et al found that Asians in Toronto, Canada had poorer preoperative function than their Caucasian counterparts.[5] Differences between different Asian ethnicities have not been well established.

Singapore has a multiracial community of Chinese (74.2%), Indians (9.5%) and Malays (13.3%)[11] and is therefore a suitable location to study differences among these Asian ethnic groups. In this study, we evaluated differences among Chinese, Indians and Malays undergoing TKA in our institution, in terms of preoperative scores and postoperative outcomes at the end of 1- and 2-years.

Materials and Methods

Study Population

With ethical approval from the National Healthcare Group Domain Specific Review Board, this retrospective observational study was conducted at the National University Hospital (a 1000-bed tertiary care institution of Singapore). From the hospital's joint arthroplasty registry, we identified all Chinese, Malay and Indian patients with primary knee OA who underwent TKA from January 2009 to June 2011. Patients with secondary knee OA (i.e. traumatic, infectious, inflammatory, metabolic) were excluded from this study.

Demographic Variables

Patients' clinical characteristics such as age, gender, ethnicity, BMI, presence of comorbidities (diabetes mellitus [DM], hypertension [HTN] and ischaemic heart disease [IHD]), were recorded. Preoperative knee range of motion (ROM) and deformity (valgus/varus) were also assessed.

Functional Assessments

All patients agreeable for TKA were asked to complete preoperative questionnaires and their knee function was objectively measured. These assessments were repeated during the follow-up visits at 1- and 2-years postoperatively. The following functional scores were measured: 1) The Knee Society Score (KSS) with its 2 components: KSS Knee Score is determined through patient's reported knee pain and the physical examination of the knee, and a KSS Function Score rates the patient's ability to walk and climb stairs. Each score ranges from 0 (worst) to 100 (best); 2) Short Form-36 Health Survey of Mental Component Score (SF 36-MCS) and Physical Component Score (SF 36-PCS) measure functional health and well-being scores that are computed to provide a physical and mental summary component. Each score ranges from 0% (worst) to 100% (best); and 3) The Western Ontario and McMaster Universities OA Index (WOMAC) Score assesses the burden of knee OA in terms of pain, stiffness and physical ability to perform various daily activities. As done by other authors,[12-14] the scoring system was transformed and normalised from the original to give a range from 0 (worst) to 100 (best).

All the above functional scores were administered by a trained research nurse blinded to our study. Knee ROM and fixed flexion deformity were objectively measured with a goniometer by the same research nurse.

Statistical Analysis

We tabulated the demographics and dependent variables of our patients and presented them in frequency tables with appropriate descriptive statistics. Categorical variables were presented as proportions and continuous variables were presented as means with standard deviation. To analyse for ethnic differences in demographics, the chi-squared test was used for comparing categorical variables (comorbidities), while student's t-test and analysis of variance (ANOVA) were used to compare continuous variables (age and BMI). In assessing for ethnic differences in our dependent variables, the chi-squared test was used to analyse categorical variables (such as gender or comorbidities), while student's t-test and

ANOVA were used to compare the means of continuous dependent variables (preoperative functional scores and knee ROM). Statistical significance was accepted with *P* value <0.05. Data analysis was performed using SPSS (SPSS Inc., Chicago IL, Version 18.)

Results

Out of 737 patients identified from the database, 229 were excluded with incomplete preoperative or postoperative functional outcome data, to avoid reporting bias. The remaining 508 patients with complete data who fulfilled the inclusion criteria were reviewed and their demographics (Table 1) and outcome scores were analysed (Table 2).

Demographic Variables (Table 1)

The ethnic breakdown revealed 388 Chinese (76.4%), 47 Malay (9.3%), and 73 Indian (14.4%) patients. The average age of Chinese patients (65.6) and Indian patients (64.3) was higher than the average age of the Malay group (60.3) (*P* <0.001). BMI was similar between Malays and Indians (with both more than the Chinese patients [*P* <0.001]). The prevalence of HTN and IHD was similar but DM was more common in Indians, which almost reached statistical significance (*P* = 0.05).

Preoperative knee ROM and knee joint alignment angle did not show statistically significant difference amongst the 3 groups.

Preoperative and Postoperative Scores (Table 2)

SF36 Physical Component Score

Preoperatively, all 3 ethnic groups had similar scores, but Chinese scored more than Malays and this was shown to be statistically significant (*P* = 0.017). At 1-year postoperatively, all 3 ethnic groups improved in this scoring, but Indians improved the least and scored less than both the Chinese and Malays, with statistical significance, (*P* = 0.002 and *P* = 0.013, respectively). At 2-years postoperatively, there was no difference between Malays and Indians. However, the Chinese still scored higher than the Indians (*P* = 0.013).

SF36 Mental Component Score

At all measured time-points, there was no significant difference in scores between the groups.

KSS Knee Score

Preoperatively, there was no significant difference in scores recorded in Chinese, Malays and Indians. At 1-year postoperatively, there was a large improvement in KSS Knee Scores seen in all 3 ethnic groups. However, statistical significant difference (*P* = 0.033) was seen when comparing postoperative scores between the Chinese (93.3) and Indians (90.3). At 2-years postoperatively, all 3 ethnic groups maintained similar scores as the previous year, and again the Chinese scored more than the Indians (*P* = 0.038).

Table 1. Demographics and Preoperative Knee Range of Motion and Alignment

Demographics	**Chinese, n = 388 (SD)**	**Malay, n = 47 (SD)**	**Indian, n = 73 (SD)**	**ANOVA (*P* Value)**	**Chinese vs Malay (*P* Value)**	**Malay vs Indian (*P* Value)**	**Chinese vs Indian (*P* Value)**
Age	65.6 (7.8)	60.3 (9)	64.3 (9.7)	0.000 or <0.001*	0.000 or <0.001*	0.031*	0.549
BMI	26.8 (4.4)	30.2 (4.8)	29.5 (5.6)	0.000 or <0.001*	0.000 or <0.001*	1.000	0.000 or <0.001*
Preoperative FFD	5.2 (6.2)	4.7 (5.4)	4.1 (7.2)	0.360	1.000	1.000	0.491
Preoperative Flexion	107.1 (16.0)	107.6 (13.1)	108.5 (18.6)	0.796	1.000	1.000	1.000
Preoperative alignment	3.8 (6.4)	3.4 (5.2)	2.4 (7.8)	0.205	1.000	1.000	0.232
Demographics	**Chinese, n = 388**	**Malay, n = 47**	**Indian, n = 73**	**Chi-squared (*P* Value)**			
Gender, male:female	28.1:71.9	21.3:78.7	35.6:64.4	0.218			
Preoperative varus/valgus deformity, varus:valgus	79.1:20.9	80.9:19.1	67.1:32.9	0.067			
DM	97 (25%)	15 (31.9%)	28 (38.4%)	0.05			
HTN	248 (63.9%)	28 (59.6%)	38 (52.1%)	0.152			
IHD	45 (11.6%)	5 (10.6%)	12 (16.4%)	0.481			

ANOVA: Analysis of variance; BMI: Body mass index; DM: Diabetes mellitus; FFD: Fixed flexion deformity; HTN: Hypertension; IHD: Ischaemic heart disease; ROM: Range of motion; SD: Standard deviation

*Statistically significant.

Table 2. Functional Scores Preoperatively and at 1- and 2-Years Postoperatively

Parameters	Chinese, n = 388 (SD)	Malay, n = 47 (SD)	Indian, n = 73 (SD)	ANOVA (*P* Value)	Chinese vs Malay (*P* Value)	Malay vs Indian (*P* Value)	Chinese vs Indian (*P* Value)
SF-36 PCS							
Preoperation	31.7 (6.6)	28.9 (6.1)	29.8 (7.1)	0.004*	0.017*	1.000	0.078
1-year postoperation	49.8 (6.5)	50.4 (5.4)	46.9 (8.2)	0.001*	1.000	0.013*	0.002*
Change at 1-year	18.1 (7.9)	21.6 (8.2)	17.0 (9.5)	0.010*	0.021*	0.010*	0.893
2-years postoperation	49.5 (6.6)	48.8 (8.2)	47.0 (7.1)	0.016*	1.000	0.517	0.013*
Change at 2-years	17.8 (8.3)	19.9 (9.8)	17.2 (8.1)	0.202	0.326	0.258	1.000
SF-36 MCS							
Preoperation	51.2 (7.4)	50.3 (10.6)	52.4 (9.1)	0.339	1.000	0.497	0.693
1-year postoperation	56.0 (5.2)	57.0 (4.2)	56.0 (5.2)	0.435	0.603	0.867	1.000
Change at 1-year	4.9 (8.1)	6.7 (10)	3.6 (8.7)	0.145	0.453	0.149	0.760
2-years postoperation	57.1 (3.9)	57.1 (6.1)	57.0 (5.9)	0.985	1.000	1.000	1.000
Change at 2-years	5.9 (7.7)	6.8 (11.7)	4.6 (9.3)	0.328	1.000	0.488	0.651
KSS knee							
Preoperation	38.4 (14.6)	33.6 (12.1)	37.2 (11.9)	0.089	0.091	0.541	1.000
1-year postoperation	93.3 (8.9)	94.0 (8.3)	90.3 (9.4)	0.028*	1.000	0.099	0.033*
Change at 1-year	54.9 (16.5)	60.4 (14.3)	53.1 (18.9)	0.053	0.097	0.056	1.000
2-years postoperation	93.9 (9.1)	93.8 (10.0)	90.9 (12.3)	0.044*	1.000	0.324	0.038*
Change at 2-years	55.5 (16.5)	60.2 (15.9)	53.6 (19.5)	0.111	0.225	0.118	1.000
KSS function							
Preoperation	50.0 (17.0)	44.5 (18.5)	49.5 (19.0)	0.130	0.131	0.366	1.000
1-year postoperation	77.5 (16.0)	79.6 (15.4)	70.4 (19.8)	0.002*	1.000	0.009*	0.002*
Change at 1-year	27.6 (19.7)	35.1 (23.3)	20.9 (19.9)	0.001*	0.048*	0.001*	0.027*
2-years postoperation	80.1 (17.5)	80.0 (15.5)	75.7 (14.8)	0.120	1.000	0.525	0.123
Change at 2-years	30.2 (19.4)	35.5. (24.1)	26.2 (20.0)	0.043*	0.254	0.037*	0.336
WOMAC							
Preoperation	62.5 (13.5)	60.1 (11.7)	59.8 (15.0)	0.193	0.764	1.000	0.764
1-year postoperation	89.5 (7.2)	90.3 (7.7)	86.8 (9.4)	0.012*	1.000	0.043*	0.017*
Change at 1-year	27.0 (13.5)	30.2 (13.5)	27.0 (15.8)	0.322	0.408	0.654	1.000
2-years postoperation	91.4 (6.9)	92.0 (5.2)	89.6 (7.6)	0.077	1.000	0.166	0.110
Change at 2-years	28.9 (13.7)	31.9 (12.5)	29.7 (14.8)	0.365	0.491	1.000	1.000

ANOVA: Analysis of variance; KSS function: Knee Society Score of knee function; KSS knee: Knee Society Score of knee symptoms; SD: Standard deviation; SF-36 MCS: Short Form-36 Health Survey of Mental Component Score; SF-36 PCS: Short Form-36 Health Survey of Physical Component Score; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index
*Statistically significant.

KSS Function Score

Preoperatively, there was no significant difference in scores recorded in Chinese, Malays, and Indians. At 1-year postoperatively, all ethnic groups improved, but the Malays improved the most and the Indians improved the least. Statistical significance was seen with Malays scoring more than Indians ($P = 0.009$) and Chinese scoring more than Indians ($P = 0.002$). At 2-years postoperatively, while the Malays did not record any further improvement in scores, the Indians improved further over the year and the final postoperative scores at 2-years showed no significant differences between the 3 ethnic groups.

WOMAC

Preoperatively, there was no significant difference in scores recorded in Chinese, Malays, and Indians. At 1-year postoperatively, all ethnic groups improved, but the Indians again failed to improve as much. Differences of statistical significance was seen with Malays scoring more than Indians ($P = 0.043$) and Chinese scoring more than Indians ($P = 0.017$). At 2-years postoperatively, the Indians improved further over the year and the final postoperative scores at 2-years showed no significant differences between the 3 ethnic groups.

Discussion

Preoperative and postoperative outcomes of OA knee may vary among patients from the 3 ethnic groups in Singapore.

Malays undergoing TKA were on average 5 years younger than Chinese and Indians. They generally had the poorest preoperative scores (although only statistically significant for SF-36 PCS versus Chinese). They also improved the most and all their postoperative scores matched those of the Chinese at both 1- and 2-years. Poorer initial scores may partly relate to physical characteristics and social/occupational practices. Obesity was common amongst Malays and is known to aggravate knee OA symptoms especially with frequent kneeling.[15,16] Amongst Malays, kneeling is commonly practiced during Muslim prayers. Malays in Singapore are also more likely to undertake moderate-to-high intensity occupations in Singapore[17,18] and such occupations are known aggravators of knee OA symptoms.[19] However, we are unable to confirm the above factors, as data on occupational and religious practices was not collected.

Indians improved less in the first year, and had lower postoperative scores (SF36 PCS, KSS Function and WOMAC) compared to both Malays and Chinese. However, they continued to improve and at 2-years, reduced this difference.

In a similar Singaporean study,[20] Chinese had better preoperative scores for KSS Knee, KSS Function and SF36. Malays showed the most improvement at 2-years for all outcome scores and showed no difference in scores from Chinese at 2-years except for SF36 Physical Function and KSS Function. Indians scored the worst at 2-years for all outcomes and this was statistically significant when compared to Chinese but not Malays.

The findings of our study and those of Siow et al[20] indicate that Malays present with the worst preoperative scores but show the most improvement after TKA, such that their postoperative scores are comparable to Chinese patients. Although Siow et al[20] found that Indians do not show as much improvement in outcome scores after TKA as Chinese and Malays (and end up with the worst outcome scores), we found that while this is the case for 1-year postoperatively, Indians continue to improve and eventually "catch up" with Chinese and Malays at 2-years.

The strength of our study lies in the relatively large sample size with similar ethnic composition to the Singapore population.[11] In addition, our patients' preoperative scores were taken from a prospectively-kept functional scoring database maintained by research nurses blinded to our study. To our knowledge, this is one of the first and largest studies to examine the evolution of preoperative and postoperative outcomes (at both 1- and 2-years) amongst Asian patients with knee OA undergoing TKA.

There are, however, several limitations in our study. Firstly, the sourcing of patients from a single tertiary referral centre might be a potential source of selection bias, as the study sample may not match the national population demographics in all respects.

Secondly, we had to exclude 229 out of 737 patients, due to incomplete data sets. Although the ethnic distribution of the exclusions (79% Chinese, 8.7% Malays and 12.3% Indians) was similar to the analysed population, the large dropout may have influenced study findings.

Thirdly, the SF-36 scoring systems were not available in the Malay and Tamil languages. Using them to assess functional scores in Malay and Indian patients with poor command of the English language might introduce some observational bias. However, we reduced this risk by engaging our hospital's translator services.

Lastly, as this was a retrospective study, our results cannot be used to establish causality between ethnicity and our dependent variables. Differences in TKA outcomes are multifactorial, and socioeconomic factors should also be assessed to explain differences between the ethnic groups. However, socioeconomic data was not part of the registry data collection. As a result, we were unable to assess the influence of socioeconomic factors on our results. Nonetheless, the findings of our study indicate that differences in preoperative function and postoperative outcomes after TKA exist among the ethnic groups in Singapore. Further research should therefore be carried out to determine if indeed socioeconomic and occupational factors account for these differences.

Conclusion

In conclusion, TKA results in significant improvements in postoperative functional outcomes in patients from the 3 major ethnic groups in Singapore. The following patterns were observed: Malays appear to present with worse preoperative scores and undergo surgery at a younger age, compared to Chinese and Indians. However, at 1-year postoperatively, Malays improve the most while Indians improve the least. Indians improve further over the second year to eventually match the Malays and Chinese. Further research is needed to determine the underlying reasons for these interethnic differences.

REFERENCES

1. Petersson IF. Occurrence of osteoarthritis of the peripheral joints in European populations. Ann Rheum Dis 1996;55:659-61.
2. Buckwalter JA, Lohmander S. Operative treatment of osteoarthrosis. Current practice and future development. J Bone Joint Surg Am 1994;76:1405-18.

3. Callahan CM, Drake BG, Heck DA, Dittus RS. Patient outcomes following tricompartmental total knee replacement. A meta-analysis. JAMA 1994;271:1349-57.
4. Norman-Taylor FH, Palmer CR, Villar RN. Quality-of-life improvement compared after hip and knee replacement. J Bone Joint Surg Br 1996;78:74-7.
5. Gandhi R, Razak F, Mahomed NN. Ethnic differences in the relationship between obesity and joint pain and function in a joint arthroplasty population. J Rheumatol 2008;35:1874-7.
6. Braga L, Renner JB, Schwartz TA, Woodard J, Helmick CG, Hochberg MC, et al. Differences in radiographic features of knee osteoarthritis in African-Americans and Caucasians: the Johnston county osteoarthritis project. Osteoarthritis Cartilage 2009;17:1554-61.
7. Wise BL, Niu J, Yang M, Lane NE, Harvey W, Felson DT, et al. Patterns of compartment involvement in tibiofemoral osteoarthritis in men and women and in whites and African Americans. Arthritis Care Res 2012;64:847-52.
8. Groeneveld PW, Kwoh CK, Mor MK, Appelt CJ, Geng M, Gutierrez JC, et al. Racial differences in expectations of joint replacement surgery outcomes. Arthritis Rheum 2008;59:730-7.
9. Lavernia CJ, Alcerro JC, Rossi MD. Fear in arthroplasty surgery: the role of race. Clin Orthop 2010;468:547-54.
10. Joshy S, Datta A, Perera A, Thomas B, Gogi N, Kumar Singh B. Ethnic differences in preoperative function of patients undergoing total knee arthroplasty. Int Orthop 2006;30:426-8.
11. Singapore Department of Statistics. Census of population, 2010. Available at: https://www.singstat.gov.sg/docs/default-source/default-document-library/publications/publications_and_papers/cop2010/census_2010_release1/cop2010sr1.pdf. Accessed on 1 September 2017.
12. Nashi N, Hong CC, Krishna L. Residual knee pain and functional outcome following total knee arthroplasty in osteoarthritic patients. Knee Surg Sport Tr A 2015;23:1841-7.
13. Quintana JM, Escobar A, Bilbao A, Arostegui I, Lafuente I, Vidaurreta I. Responsiveness and clinically important differences for the WOMAC and SF-36 after hip joint replacement. Osteoarthritis Cartilage 2005;13:1076-83.
14. Lingard EA, Katz JN, Wright RJ, Wright EA, Sledge CB. Validity and responsiveness of the Knee Society Clinical Rating System in comparison with the SF-36 and WOMAC. J Bone Joint Surg Am 2001;83-A:1856-64.
15. Vulcano E, Lee YY, Yamany T, Lyman S, Valle AG. Obese patients undergoing total knee arthroplasty have distinct preoperative characteristics: an institutional study of 4718 patients. J Arthroplasty 2013;28:1125-9.
16. Coggon D, Croft P, Kellingray S, Barrett D, McLaren M, Cooper C. Occupational physical activities and osteoarthritis of the knee. Arthritis Rheum 2000;43:1443-9.
17. Hughes K, Yeo PP, Lun KC, Thai AC, Wang KW, Cheah JS. Physical activity in Chinese, Malays and Indians in Singapore. Ann Acad Med Singapore 1990;19:326-9.
18. Khaing Nang EE, Khoo EY, Salim A, Tai ES, Lee J, Van Dam RM. Patterns of physical activity in different domains and implications for intervention in a multi-ethnic Asian population: a cross-sectional study. BMC Public Health 2010;10:644.
19. McWilliams DF, Leeb BF, Muthuri SG, Doherty M, Zhang W. Occupational risk factors for osteoarthritis of the knee: a meta-analysis. Osteoarthritis Cartilage 2011;19:829-39.
20. Siow WM, Chin PL, Chia SL, Lo NN, Yeo SJ. Comparative demographics, ROM, and function after TKA in Chinese, Malays, and Indians. Clin Orthop 2013;471:1451-7.

Nadir Zahir Shah, [1]*MS (Orth)*, Rishi Malhotra,[1]*BMBS, MRCS-Eng*, Choon Chiet Hong,[1]*MBBS, MRCS-Ed*, Jonathan BY Sng,[1]*MBBS*, Chee Hoe Kong, [1]*MBBS*, Liang Shen, [2]*PhD*, Nazrul Nashi,[1]*MBBS*, Lingaraj Krishna, [1]*MBBS, MRCSEd, FRCSEd (Orth)*

[1]University Orthopaedics, Hand and Reconstructive Microsurgery Cluster, National University Health System, Singapore
[2]Department of Biostatistics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

Address for Correspondence: Dr Rishi Malhotra, University Orthopaedics, Hand and Reconstructive Microsurgery Cluster, National University Health System, 5 Lower Kent Ridge Road, Singapore 119228.
Email: rishi_malhotra@nuhs.edu.sg

ANNALS

Official Journal of the Academy of Medicine, Singapore

Call for Papers

The Annals is the official journal of the Academy of Medicine, Singapore. Established in 1972, Annals is the leading medical journal in Singapore which aims to publish novel findings from clinical research as well as medical practices that can benefit the medical community.

Published monthly, online, open-access and peer-reviewed, Annals is indexed in Index Medicus, Science Citation Index – Expanded, ISI Alerting Services, and Current Contents/ Clinical Medicine.

Annals invites medical professionals to publish their research papers in the journal. After an initial review by the editorial board, those manuscripts that meet specifications will be sent to the reviewers. Papers of sufficient merits will be published. Authors will also be notified if their manuscripts are deemed not suitable for publication.

For guidance on manuscript preparation, authors are advised to read the instructions to author. The guidelines for publication of all categories of articles published in the journal can be found at: http://www.annals.edu.sg/pdf/Guidelines_for_Publication.pdf.

For submission of manuscript, please visit http://www.annals.edu.sg/OnlineManuscript/. If you have any queries about manuscript submission, please email annals@ams.edu.sg.

ANNALS, ACADEMY OF MEDICINE, SINGAPORE
81 Kim Keat Road, #11-00 & #12-00 NKF Centre, Singapore 328836
Tel: +65 6593 7800 | Fax: +65 6593 7867 | E-mail: annals@ams.edu.sg | Homepage: http://www.annals.edu.sg