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*"If your heart is a volcano, how shall you
expect flowers to bloom?"*

Khalil Gibran (1883 – 1931)
Lebanese poet

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Unprofessional Doctors—Are They Really Born This Way?

Caroline CP Ong,¹ MBBS, FRCS, FAMS, Nigel CK Tan,² MBBS, FRCP, MHPed

- Ms M, a third-year medical student, posts a derogative comment on her Facebook account about a patient undergoing her fourth termination of pregnancy.
- Dr R, a junior resident, yells on the phone, “I’m arranging an urgent CT scan, stop calling me about stupid ward changes!”
- Mr S, a senior surgeon, slaps the hand of the scrub nurse when she hands him the wrong instrument.
- Dr P, a senior physician responsible for hospital purchasing decisions, travels frequently on industry-sponsored trips to conferences.

Framing the Discussion: Why Are Professionals Not Always Professional?

Professionalism has traditionally been viewed as an integral component of the practice of medicine, whereby a good doctor is always “professional”. Modern day preoccupation with the “problem of professionalism”¹ reflects the medical fraternity’s increasing concern about breaches of professionalism and commercialisation of medicine. Despite good evidence that unprofessional behaviour negatively impacts patient care,² it often remains unchecked and unreported.

The concept of medical professionalism has evolved in recent years. The nostalgic view³ of professionalism regarded it as a set of attributes inherent within an individual. Responses to lapses of professionalism therefore tend to focus on the individual—is the individual behaving aberrantly? Did the residency select the wrong candidate?

New concepts about professionalism move beyond the individual. They recognise that multiple factors contribute to the individual’s behaviour within a complex adaptive system.³ This complexity systems approach helps us understand why we need to look beyond “picking the right people”, as factors within the system can influence an individual’s professional behaviour.

Therefore, teaching doctors about the medical profession’s

core values and behaviours is not enough. They also need to learn professional resilience skills to cope with the system’s demands.¹ At the system level, healthcare organisations should examine their processes to reduce conflicts and challenges to professionalism faced by the healthcare providers working within these systems.

How to Be Professional?

Learning to become and stay professional in the workplace requires the healthcare provider to understand what is meant by professionalism and develop the necessary skills to maintain professionalism. Codes or frameworks that define behaviours therefore help to make explicit the values of professionalism.⁴ The student needs to acquire basic skills of communication, teamwork and clinical competence to behave professionally.⁵

Additionally, other challenges that conflict with the individual’s desire to be professional may arise in the workplace. To face such challenging situations, the student needs to develop additional skills for professional resilience: self-awareness, self-control, situational awareness, alternative strategy development, crisis communication skills, and peer coaching.¹

How Do We Teach Professionalism?

Formal Curriculum

Universities and residency programmes already recognise the need for a formal professionalism curriculum for medical students and residents. Institutions who value patient safety should also promote continuing professionalism in faculty development programmes.^{5,6} Inter-professional education where doctors, nurses and allied health train together helps enhance performance of teams that work together. Innovative methods to incorporate professionalism and continuing medical education (CME) into departmental meetings include the use of ethics case discussions or structured morbidity and mortality meetings. Residency

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programmes could introduce a work-based assessment like the performance measurement evaluation matrix (PMEX) tool⁷ to highlight the importance of professionalism by aligning assessment with learning objectives.

Hidden Curriculum

Regardless of the official policy on expected professional behaviours, it must be reflected in the actions of staff on the ground, otherwise the hidden curriculum (unplanned learning through observation) will override any formal training programme. A senior doctor who routinely role-models respectful interactions with colleagues, nurses and juniors sends a powerful message to the rest of the team about professionalism. Clinical teachers who witness unprofessional acts by trainees should give explicit feedback, as indirect responses using humour or non-verbal disapproval may be missed by the learner.⁸

System Strategies

There are various strategies the institution can employ to reduce unprofessional behaviour. Junior nurses and doctors feel threatened when they experience bullying or witness disruptive behaviours of senior staff going unchecked. An institution protocol that trains staff to show the T-sign to signify time-out⁶ or a similar verbal/visual reminder to halt the behaviour empowers the victim and prevents escalation of bad behaviour. The time-out forces the abusive person to reflect and provides an opportunity to regain emotional self-control.

Peer pressure can be harnessed by training all staff to have “a cup-of-coffee conversation”,⁶ as the occasional individual with poor social skills may be oblivious to the effects of his/her actions. In other situations, a person displaying unprofessional behaviour may be under external stress or just “having a bad day”. An informal talk provides peer support and reinforces the institutional behaviour norms.

Finally, supervisors often feel uncomfortable confronting problem doctors, especially their peers. Practical guides for the problem trainee⁹ or doctor¹⁰ assist in working out the potential predisposing causes for the behaviour (e.g. mental/physical illness, personality, emotional, substance dependence, life changes, team or systems issues) and delineate the necessary steps of counselling, remediation and documentation.

Remove Systemic Barriers to Professionalism

Leaders in society and organisations should examine the system to remove barriers and conflicting demands on the individual. Within the clinical environment, excessive workload and fatigue are major stressors. Adequate

manpower and regular review of work-processes prevent unprofessional behaviour related to poor decision-making and reduced emotional control caused by fatigue and rushing. Introducing standardised protocols for handover and communication minimises miscommunication errors that trigger conflict. Ensuring clarity of roles and responsibilities between different healthcare providers working in teams will reduce conflict between team members.

Remuneration of individuals typically drives their behaviours. Appropriate compensation rather than a “fee-for-service” model reduces unethical overcharging and unnecessary procedures. Pharmaceutical sponsorship for medical conference attendance becomes less attractive when organisations provide funding for continued professional development. Lifestyle considerations like work-life balance are increasingly important for the younger generation, so consider structuring work schedules to remove tension between work and personal or family needs.

Conclusion

Lapses in professionalism are no longer just about “the problem trainee” or “the rude doctor”. The complex adaptive system view of professionalism illustrates the multi-faceted approach needed to develop the culture of professionalism in the clinical environment. This approach encompasses training of staff at all levels to understand and develop the necessary skills, having deliberate structures and protocols to deal with unprofessional behaviours, and eliminating systemic barriers. It is time we reframed our views about professionalism.¹

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High Glycaemic Index (GI) of Asian Diet—What are the Clinical Implications?

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Traditional Asian diets are characterised and dominated by high-glycaemic carbohydrates^{1,2} with primarily rice as the staple grain. Studies have shown that Asian rice, rice porridge, and glutinous (sticky) rice are extremely high in glycaemic index (GI).³ Plain rice has a high GI value of approximately 80,¹ which elicits postprandial glucose responses close to that of pure glucose.³ Because rice and high GI foods are consumed in high amounts, the Asian diet is naturally high in glycaemic load (GL = GI x grams of carbohydrates). Even with rapid modernisation and increase in the intake of fats and protein, carbohydrates still accounted for more than 50% of the total calorie intake in the Asian Chinese populations.⁴

The glycaemic index and glycaemic load reflect the nature of carbohydrates in causing rapid postprandial increase in blood glucose and insulin levels,⁵ which have been consistently recognised to contribute to adversely impact a variety of metabolic risk factors. Studies in both animals⁶ and humans^{5,7} have shown a positive association of a high GI/GL diet with weight gain and obesity. A high GI/GL diet has similarly been shown to be positively associated with higher levels of serum triglycerides, low-density lipoprotein (LDL) cholesterol levels, and serum coagulation factors.^{5,8} Hyperinsulinaemia resulting from a high GI/GL diet may stimulate ovarian secretion of androgens, leading to adverse metabolic consequences with increased risk of developing type 2 diabetes in women.⁹ Resulting from the above-mentioned mechanisms, a high GI/GL diet has been shown to adversely affect glycaemic control in individuals with diabetes¹⁰ and being associated with greater risk of developing type 2 diabetes,¹¹ coronary heart disease,¹² and stroke¹³ in prospective studies.

Whilst a high-glycaemic Asian diet did not formerly contribute to disease in an active and lean population, such a diet has important implications in the modernising Asian societies characterised by increasing rates of adiposity and sedentary lifestyle particularly in the urban regions.^{14,15}

This is due to an important biologic synergy in which high GI diet elicits significantly greater adverse risks among overweight and sedentary populations.¹⁵ A significantly stronger effect on the development of type 2 diabetes,¹¹ coronary heart disease,^{12,16} and stroke¹³ have been noted among those with greater adiposity (body mass index (BMI) >23 or BMI >25). High GL has also been observed to be more strongly associated with colorectal cancer incidence among those with higher BMI,¹⁷ and high-glycaemic sugar-sweetened beverages more strongly linked with pancreatic cancer among those with low physical activity and/or greater adiposity.¹⁸ This synergistically increased adverse risk has been attributed to the deteriorating state of insulin resistance and glucose control in overweight individuals, who are more susceptible and prone to uncontrolled postprandial hyperglycaemia after glucose challenge from a high-glycaemic meal.¹⁶ Many Asian populations have a higher total and central adiposity for a given body weight when compared with matched white populations.¹⁴ A higher prevalence of metabolic syndrome in South and Southeast Asians is mostly attributed to the higher prevalence of central adiposity with its associated increased visceral fat mass.^{14,19} Visceral fat increases the risk of diabetes and hyperlipidaemia by increasing insulin resistance.²⁰ Evidence from clinical trial indicates that a high GI diet induces a sequence of hormonal and metabolic changes that promote excessive food intake in obese individuals,²¹ adding to the vicious cycle with the effect of excess calorie intake, a risk factor for a vast majority of chronic diseases.

With rapid modernisation, populations in many Asian countries have gone on to adopt lifestyle and dietary patterns of the West. The consumption of added sugars, particularly in the form of sugar-sweetened beverages like soda and fruit drinks, are accompanying and compounding the traditional high-glycaemic carbohydrate diet. A comparative analysis of more than 100 countries, indicates that from 1962 to 2000, consumption of added sugars has increased

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globally.²² High-fructose corn syrup, the primary sweetener found in sugared beverages, has been shown to induce rapid and dramatic spikes in blood glucose and insulin concentrations.²³ Consumption of such high-glycaemic sugar-sweetened beverages has been consistently associated with increased systemic inflammation,²⁴ weight gain,²⁵ increased risk of obesity and type 2 diabetes as a result of its high-glycaemic properties.¹¹

The recent obesity epidemic in many Asian countries¹⁴ bodes ominously for increased risk of chronic disease by virtue of adiposity itself, but also predicts a rising tide of even greater adverse compounding risk from a high-glycaemic diet.

The high GI staple diet in many Asian countries will become an even greater public health concern as it will compound the adverse effects of increasing adiposity, leading to dramatically increased cardiometabolic risks.¹⁵ There is enormous cost to society from the resultant diabetes and cardiovascular morbidity.²⁶ These effects will be felt most dramatically in Asian countries with the fastest growing obesity epidemic like China and India.¹⁴ It is imperative that the governments of these affected Asian countries initiate public health programmes urgently to reverse the tide of the emerging obesity epidemic in their countries, thereby to pre-emptively defuse the enormous compounding health risks stemming from the negative convergence of obesity with a high GI Asian diet.¹⁵

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Antibiotic Therapy and Clinical Outcomes of *Pseudomonas Aeruginosa* (PA) Bacteraemia

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Abstract

Introduction: *Pseudomonas aeruginosa* (PA) bacteraemia is associated with high morbidity and mortality. We assessed clinical outcomes in patients with PA bacteraemia treated with piperacillin-tazobactam (TZP) versus other antibiotics, and monotherapy versus combination, all with proven activity by disc testing without minimum inhibitory concentration (MIC) data. **Materials and Methods:** All patients with PA bacteraemia in 2007 to 2008 were reviewed for demographic, comorbidity, clinical, laboratory, treatment and outcome data. Primary outcome was 30-day mortality. Secondary outcomes included microbiological clearance, clinical response and length of stay (LOS). **Results:** Median age for 91 patients was 65 years. Median Simplified Acute Physiology Score (SAPS) II score was 30. Monotherapy was used in 77 cases: 42 on ceftazidime, 17 on TZP, 10 on carbapenems, and 8 on other antipseudomonal antibiotics. The 30-day mortality was 20.9%, and similar between ceftazidime and TZP versus other antibiotics respectively. More patients in combination versus monotherapy group had cardiovascular diseases, diabetes mellitus and vascular access as source of bacteraemia. Patients on monotherapy had higher 30-day mortality (24.7% vs 0%, $P = 0.037$). Multivariate analysis identified SAPS II score (OR = 1.097, 95% CI, 1.032 to 1.166, $P = 0.003$) and cancer (OR = 4.873, 95% CI, 1.235 to 19.223, $P = 0.024$) as independent predictors of 30-day mortality. **Conclusion:** TZP appeared to be an effective culture-guided antibiotic for PA bacteraemia. High 30-day mortality in monotherapy might be confounded by comorbidity, illness severity and sample size. Cancer patients and a high SAPS II score were independent predictors of 30-day mortality.

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Key words: Bloodstream infections, Mortality

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Abstract

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Introduction

Pseudomonas aeruginosa (PA) is a virulent nosocomial pathogen and PA bacteraemia is associated with high mortality ranging from 18% to 59%.¹⁻⁷ It is ranked among the top 3 gram-negative bacteria associated with bacteraemia.^{3, 8-10} It is commonly reported in patients with cancer^{3,11,12} and in intensive care units (ICUs).^{8,10} PA bacteraemia commonly arises from urinary source,^{7,12-15} pneumonia^{7,12-15} and vascular access devices.^{7,13}

Inappropriate empirical or delayed active antibiotic worsens clinical outcomes in patients with PA bacteraemia.^{2-5,7,15}

Mathematical modeling has shown that target attainment for optimal bacterial killing is unlikely if minimum inhibitory concentration (MIC) for piperacillin-tazobactam (TZP) exceeded 32 µg/mL.^{16,17} Subsequently, a clinical study confirmed higher mortality for TZP if MIC exceeded 32 µg/mL in severely ill patients.¹⁶ Another study showed that empirical TZP was associated with increased mortality for PA bacteraemia with MIC 32 to 64 µg/mL.⁶ Consequently, the MIC breakpoint for non-susceptibility for TZP against PA was revised from 64 µg/mL to 16 µg/mL in 2012.

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However, MIC information was not routinely available to doctors, a situation we encountered at Tan Tock Seng Hospital (TTSH), Singapore.

Many studies reported no difference in outcomes between monotherapy and combination antibiotic therapy.^{2,7,15,18,19} A meta-analysis of randomised controlled trials in febrile neutropenia²⁰ and another in immunocompetent patients²¹ concluded that combination antibiotics were not better than monotherapy for PA infections, although both analyses conceded that the numbers were small. Subsequently, a meta-analysis of observational studies concluded that combination therapy was more effective than monotherapy²² although this was biased by aminoglycoside as monotherapy.²³ A review on PA pneumonia recently recommended 3 to 5 days of combination antibiotic based on the available evidence.²⁴

Therefore we performed a 2-year retrospective study of PA bacteraemia with the objectives of: (i) determining clinical outcomes of treating PA bacteremia with various antipseudomonal antibiotics with proven activity by disc testing without MIC data, and (ii) comparing monotherapy versus combination therapy.

Materials and Methods

Study Cohort

This retrospective study was conducted in TTSH, a 1400-bed university teaching hospital in Singapore. We identified all patients with PA bacteraemia from 1 January 2007 to 31 December 2008 from our microbiology database. The study was conducted before the change in MIC breakpoint for TZP in PA from 64 to 16 µg/mL. Our inclusion criteria were: (i) patients who received at least 2 days of culture-guided antibiotics for the positive blood culture, and (ii) first episode of PA bacteraemia in the study period. Our exclusion criteria were: (i) patients with incomplete data, and (ii) patients with unavailable medical records.

Data Collection

The following data were collected retrospectively from the hospital medical records: age; gender; race; comorbidities; use of devices; severity of illness in terms of Simplified Acute Physiology Score II (SAPS II)²⁵ and Pitt bacteraemia score;²⁶ whether doses of antibiotics used were appropriate; surgery in the last 30 days; prior admission to ICU; length of stay (LOS) in TTSH; other microorganisms found in blood; empirical and culture-guided antibiotics.

Definitions

The presence of PA bacteraemia was defined as the identification of PA in blood culture. Severity of disease was determined by Pitt bacteraemia score²⁶ and SAPS II score.²⁵

Parameters within each scoring system were determined within 24 to 48 hours before index culture.⁵ If the exact Glasgow Coma Scale (GCS) score was unavailable, the GCS score would be defined by the clinician description in the case notes, for example, alert: 14 to 15, confused: 11 to 13, drowsy: 7 to 10, unresponsive: ≤6.²⁷

Nosocomial infection was defined as infection that occurred more than 48 hours after hospital admission. Healthcare-associated infection was defined as infection that occurred in less than 48 hours after admission in patients previously admitted to other hospitals or stayed in nursing homes or other community hospitals in the past 3 months. Community-acquired infection was defined as infection that occurred in less than 48 hours without previous admission to hospitals, nursing homes or community hospitals in the past 3 months. Polymicrobial bacteraemia was defined as the presence of more than 1 micro-organism in the blood culture. Active empirical therapy was defined as antibiotic therapy active against PA given prior to culture results. Active definitive therapy was defined as the first antibiotic active against PA given for at least 2 days after culture results were available. Combination therapy was the use of 2 or more active antibiotics overlapping for more than 48 hours throughout the entire treatment duration. Doses of antibiotics ordered were checked against drug references such as Lexi-comp®. They were deemed as appropriate if the dosing adjustments were according to the renal function as per the drug reference for PA bacteraemia.

The primary outcome was 30-day mortality. Secondary outcomes included LOS, clinical and microbiological response by day 7. Clinical response was defined as defervescence, improvement in oxygen requirement, and symptoms and signs as documented in medical charts. All outcomes were measured from the day of positive blood culture.

Statistical Analysis

The Pearson's chi-square test or Fisher's exact test was used to compare categorical variables while the Mann-Whitney U test was used for continuous variables. Univariate and multivariate analysis for 30-day mortality were carried out using binary logistic regression model. Variables that yielded *P* value less than or equal to 0.10 in the univariate analysis were included into the multivariate analysis. All the *P* values were 2-tailed and *P* < 0.05 indicated statistical significance. The Predictive Analytics Software (PASW) statistics, version 18.0 (SPSS Inc., Chicago, III), was used for this analysis. This study was approved by our institutional review board (DSRB 2009/00439).

Results

Description of the Study Cohort

Out of 120 patients with PA bacteraemia in the study period, 91 of them met the inclusion criteria (29 were excluded; 12 were excluded as these patients did not receive at least 2 days of definitive antibiotic treatment for bacteraemia, and 17 patients had either incomplete data or unavailable medical records). The median age was 65 years (range, 53 to 76 years). Males comprised 52 (57.1%). Combination antibiotic therapy was used in 14 patients (15.4%). Of those who used single definitive antibiotic therapy, ceftazidime (CAZ) was the most commonly used; 42 patients were on CAZ (46.2%), 17 were on TZP (18.7%), 10 were on carbapenems (CBP) (11.0%) and rest of the 8 patients were on other antipseudomonal antibiotics (8.8%) (3 on ciprofloxacin, 1 on polymyxin B, 2 on aminoglycoside, 1 on aztreonam, 1 on piperacillin).

Median SAPS II score was 30 (range, 22 to 38) and Pitt bacteraemia score 1 (range, 0 to 2). Forty-one (45.1%) patients had nosocomial, 29 (31.9%) healthcare-associated and 21 (23.1%) community-acquired infections. Forty-seven (51.6%) patients received appropriate antibiotic doses for PA bacteraemia. Forty (44.0%) patients received active empirical therapy, 15 patients received TZP, 9 received CBP, 7 received CAZ and the rest received other empirical antibiotics (5 on ciprofloxacin, 2 on aminoglycosides and 3 were on combination of empirical antipseudomonal antibiotics). Out of the 51 patients who did not receive active empirical antibiotics, only 3 of them did not receive any empirical antibiotics. Nineteen (20.9%) had polymicrobial bacteraemia.

Sources of bacteraemia were urinary (31.9%), skin and soft tissue (12.1%), respiratory (12.1%), and vascular access device (11.0%). In 19.8% of cases, no clear source of infection could be determined. ICU admission preceded 18.7% and surgical procedures 20.9% of PA bacteraemia. Mortality at 30 days was 20.9%. Median LOS was 20 days (range, 11 to 41 days). Clinical response occurred in 70.3% and microbiological response in 83.7% at 7 days.

Comparison of Antibiotic Treatment and Clinical Outcomes

As shown in Table 1, out of the 19 patients who died within 30 days from index bacteraemia, there were significantly more patients with cardiovascular diseases, cancer and human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) as comorbidities, and they were significantly more ill with higher median SAPS II score. Notably, there was no significant difference for individual type of antibiotic treatment.

No patient who died at 30 days was on combination antibiotics vs 19 (24.7%) on monotherapy for definitive

treatment ($P = 0.037$). Median length of hospitalisation (21 [10 to 41] vs 18 [14 to 51] days, $P = 0.458$), 7-day microbiological (41 [83.7%] vs 8 [61%], $P = 0.122$) and clinical (64 [83.1%] vs 13 [92.9%], $P = 0.687$) response did not differ between monotherapy and combination therapy. Notably, patients on combination definitive therapy had more cardiovascular diseases ($P = 0.014$), diabetes mellitus ($P = 0.004$) and vascular access as a source of bacteraemia ($P = 0.044$), versus monotherapy (Table 2).

Baseline characteristics were similar between those patients who received CAZ versus those who did not, as well as TZP vs non-TZP treatment groups (Tables 4 and 5). There was no statistically significant difference in 30-day mortality (12 [28.6%] vs 7 [20.0%], $P = 0.436$), median length of hospitalisation (18 [9 to 31] vs 25 [11 to 64] days, $P = 0.072$), 7-day microbiological (23 [92%] vs 18 [75%], $P = 0.138$) and clinical response (33 [78.6%] vs 31 [88.6%], $P = 0.243$) in CAZ versus non-CAZ treatment groups. Similarly 30-day mortality (4 [23.5%] vs 15 [25.0%], $P = 0.901$), median length of hospitalisation (20 [10 to 40] vs 21 [11 to 41] days, $P = 0.927$), 7-day microbiological (7 [63.6%] vs 34 [89.5%], $P = 0.063$) and clinical response (15 [80.2%] vs 49 [81.7%], $P = 0.721$) did not differ significantly between TZP and non-TZP treatment groups. Notably, there was no significant difference in proportions of patients who received active empirical antibiotic in monotherapy vs combination therapy, CAZ vs non-CAZ, and TZP vs non-TZP treatment groups.

Risk Factors for 30-day Mortality

Univariate analysis identified risk factors for 30-day mortality as cardiovascular disease (OR = 0.320, CI, 0.113 to 0.905, $P = 0.032$), cancer (OR = 7.200, CI, 2.252 to 23.023, $P = 0.001$), HIV/AIDS (OR = 6.133, CI, 1.241 to 30.309, $P = 0.026$) and median SAPS II score (OR = 1.091, CI, 1.040 to 1.146, $P = \leq 0.001$). On multivariate analysis, only cancer as comorbidity (OR = 4.873, CI, 1.235 to 19.223, $P = 0.024$) and median SAPS II score (OR = 1.097, CI, 1.032 to 1.166, $P = 0.003$) remained as independent predictors of 30-day mortality (Table 3).

Discussion

Studies have reported severe sepsis or shock,^{2,13,15} severity of illness,^{1,2,4-6,13,14,28} pneumonia as source,^{2,7} ineffective empirical or definitive antibiotic therapy,^{2,4,15} admission to ICU^{13,15} and age^{5,13,28} as independent risk factors for mortality. Differences in independent risk factors might be due to definition of outcome^{1,4-7,13,15,28,29} and study populations.¹⁴ In addition to published risk factors, our study also found cancer and SAPS II score as independent predictors of 30-day mortality.

Table 1. Baseline Characteristics and Antibiotic Therapy for 91 Patients with *Pseudomonas Aeruginosa* Bacteraemia with and without 30-day Mortality*

30-day Mortality	Yes n = 19	No n = 72	P Value
Age, median years (range)	66 (53 – 73)	65 (53.5 – 76.25)	0.689
Male	14 (73.7%)	38 (52.8%)	0.123
Site of Acquisition			
Nosocomial	11 (57.9%)	30 (41.7%)	0.300
Healthcare-associated	5 (26.3%)	24 (33.3%)	0.783
Community	3 (15.8%)	18 (25.0%)	0.397
Comorbidity			
Cardiovascular	8 (42.1%)	50 (69.4%)	0.034
Diabetes mellitus	5 (26.3%)	29 (40.3%)	0.300
Cancer	9 (47.4%)	8 (11.1%)	<0.001
Renal	2 (10.5%)	19 (26.4%)	0.144
HIV/AIDS	4 (21.1%)	3 (4.2%)	0.014
Respiratory	1 (5.3%)	9 (12.5%)	0.370
Source of Bacteraemia			
Urinary system	5 (26.3%)	24 (33.3%)	0.783
Unknown	6 (31.6%)	12 (16.7%)	0.147
Respiratory	4 (21.1%)	7 (9.7%)	0.178
Skin and soft tissue	2 (10.5%)	9 (12.5%)	0.814
Vascular access	0 (0.0%)	10 (13.9%)	0.085
Hepatobiliary	1 (5.3%)	5 (6.9%)	0.793
Intra-abdominal	1 (5.3%)	3 (4.2%)	0.836
Others	0 (0.0%)	2 (2.8%)	0.463
Severity of Illness			
Median SAPS II score (range)	39 (30 – 52)	28 (20.75 – 37.25)	0.010
Median Pitt bacteraemia score (range)	1 (0.5 – 2)	1 (0 – 2)	0.485
Device used†	10 (52.6%)	50 (69.4%)	0.184
Surgery in past 30 days	2 (10.5%)	17 (23.6%)	0.212
Intensive care admission	3 (15.8%)	14 (19.4%)	0.716
Polymicrobial	5 (26.3%)	14 (19.4%)	0.512
Appropriate dose	12 (63.2%)	35 (48.6%)	0.259
Active empirical therapy	11 (57.9%)	29 (40.3%)	0.200
Ceftazidime	3 (15.8%)	4 (5.6%)	0.136
Piperacillin-tazobactam	3 (15.8%)	11 (15.3%)	0.956
Carbapenems	3 (15.8%)	6 (8.3%)	0.333
Ciprofloxacin	1 (5.3%)	4 (5.6%)	0.960
Aminoglycosides	0 (0.0%)	2 (2.8%)	0.463
Combination‡	1 (5.3%)	2 (2.8%)	0.589
Definitive Antibiotic Therapy			
Ceftazidime	12 (63.2%)	30 (41.7%)	0.123
Piperacillin-tazobactam	4 (21.1%)	13 (18.1%)	0.766
Carbapenems	3 (15.8%)	7 (9.7%)	0.452
Others§	0 (0.0%)	8 (11.1%)	0.128
Combination antibiotics	0 (0.0%)	14 (19.4%)	0.037

HIV/AIDS: Human immunodeficiency virus/ Acquired immune deficiency syndrome

*Data are number of patients (%), unless stated otherwise.

†Device used included central venous catheter, peripherally inserted central catheter, arterial line, prosthetic heart valves, urinary catheter, permanent catheter for dialysis, tracheostomy tube, percutaneous transhepatic cholangiogram and percutaneous nephrostomy tube.

‡1 was on imipenem + amikacin, 1 was on ceftazidime + ciprofloxacin, 1 was on piperacillin-tazobactam + amikacin.

§Ciprofloxacin = 3, polymyxin = 1, aminoglycoside = 2, piperacillin = 1, aztreonam = 1.

|| Carbapenem + aminoglycoside = 2, ceftazidime + aminoglycoside = 4, ceftazidime + ciprofloxacin = 3, piperacillin-tazobactam + aminoglycoside = 1, piperacillin-tazobactam + ciprofloxacin = 2, aminoglycoside + ciprofloxacin = 1, carbapenem + aminoglycoside + ciprofloxacin = 1.

Table 2. Baseline Characteristics of Patients with *Pseudomonas Aeruginosa* Bacteraemia Who Received Active Definitive Therapy (Monotherapy versus Combination Antibiotic Therapy)*

Variable	Monotherapy n = 77	Combination n = 14	P Value
Age, median years (range)	65 (52 – 76)	67 (57 – 76)	0.552
Male	46 (59.7%)	6 (42.9%)	0.240
Site of Acquisition			
Nosocomial	35 (45.5%)	6 (42.9%)	0.857
Healthcare-associated	24 (32.2%)	5 (35.7%)	0.761
Community	18 (23.4%)	3 (21.4%)	1.000
Comorbidity			
Cardiovascular	45 (58.4%)	13 (92.9%)	0.014
Diabetes mellitus	24 (31.2%)	10 (71.4%)	0.004
Cancer	15 (19.5%)	2 (14.3%)	1.000
Renal	15 (19.5%)	6 (42.9%)	0.082
HIV/AIDS	7 (9.1%)	0 (0.0%)	0.590
Respiratory	8 (10.4%)	2 (14.3%)	0.649
Source of Bacteraemia			
Urinary system	25 (32.5%)	4 (28.6%)	1.000
Unknown	18 (23.4%)	0 (0.0%)	0.064
Respiratory	11 (14.3%)	0 (0.0%)	0.203
Skin and soft tissue	7 (9.1%)	4 (28.6%)	0.062
Vascular access	6 (7.8%)	4 (28.6%)	0.044
Hepatobiliary	5 (6.5%)	1 (7.1%)	1.000
Intra-abdominal	3 (3.9%)	1 (7.1%)	0.494
Others	2 (2.6%)	0 (0.0%)	1.000
Severity of Illness			
Median SAPS II score (range)	30 (22 – 39)	32 (24 – 38)	0.912
Median Pitt bacteraemia score (range)	1 (0 – 2)	1 (0 – 2)	0.300
Device used†	49 (63.6%)	11 (78.6%)	0.366
Surgery in past 30 days	17 (22.1%)	2 (14.3%)	0.726
Intensive care admission	14 (18.2%)	3 (21.4%)	0.721
Polymicrobial	15 (19.5%)	4 (28.6%)	0.480
Active empirical therapy	34 (44.2%)	6 (42.9%)	0.928

HIV/AIDS: Human immunodeficiency virus/ Acquired immune deficiency syndrome

*Data are number of patients (%), unless stated otherwise.

†Device used included central venous catheter, peripherally inserted central catheter, arterial line, prosthetic heart valves, urinary catheter, permanent catheter for dialysis, tracheostomy tube, percutaneous transhepatic cholangiogram and percutaneous nephrostomy tube.

Table 3. Multivariate Analysis of Risk Factors for 30-day Mortality in *Pseudomonas Aeruginosa* Bacteraemia

Variable	Univariate Analysis		Multivariate Analysis	
	Odds Ratio (95% CI)	P Value	Adjusted Odds Ratio (95% CI)	P Value
Cardiovascular (comorbidity)	0.320 (0.113 – 0.905)	0.032	-	-
Cancer	7.200 (2.252 – 23.023)	0.001	4.873 (1.235 – 19.223)	0.024
HIV/AIDS	6.133 (1.241 – 30.309)	0.026	-	-
Median SAPS II score	1.091 (1.040 – 1.146)	<0.001	1.097 (1.032 – 1.166)	0.003
Ceftazidime (definitive monotherapy)	2.400 (0.846 – 6.812)	0.100	-	-

HIV/AIDS: Human immunodeficiency virus/ Acquired immune deficiency syndrome

Table 4. Baseline Characteristics of Patients with *Pseudomonas Aeruginosa* Bacteraemia Who Received Active Definitive Therapy (CAZ versus Non-CAZ Treatment)*

Variable	CAZ n = 42	Non-CAZ n = 35	P Value
Age, median years (range)	65 (53 – 74)	65 (51 – 77)	0.918
Male	24 (57.1%)	22 (62.9%)	0.611
Site of Acquisition			
Healthcare-associated	14 (33.3%)	10 (28.6%)	0.653
Nosocomial	16 (38.1%)	19 (54.3%)	0.155
Community	12 (28.6%)	6 (17.1%)	0.238
Comorbidity			
Cardiovascular	24 (57.1%)	21 (60.0%)	0.800
Diabetes mellitus	14 (33.3%)	10 (28.6%)	0.653
Respiratory	3 (7.1%)	5 (14.3%)	0.457
Cancer	11 (26.2%)	4 (11.4%)	0.103
Renal	8 (19.0%)	7 (20.0%)	0.916
HIV/AIDS	4 (9.5%)	3 (8.6%)	1.000
Source of Bacteraemia			
Hepatobiliary	3 (7.1%)	2 (5.7%)	1.000
Intra-abdominal	1 (2.4%)	2 (5.7%)	0.588
Vascular access	2 (4.8%)	4 (11.4%)	0.402
Respiratory	7 (16.7%)	4 (11.4%)	0.513
Skin and soft tissue	3 (7.1%)	4 (11.4%)	0.695
Urinary system	17 (40.5%)	8 (22.9%)	0.100
Unknown	9 (21.4%)	9 (25.7%)	0.658
Others	0 (0.0%)	2 (5.7%)	0.203
Severity of Illness			
Median SAPS II score (range)	29 (22 – 39)	30 (22 – 44)	0.846
Median Pitt bacteraemia score (range)	1 (0 – 2)	2 (0 – 3)	0.167
Device used†	26 (61.9%)	23 (65.7%)	0.729
Surgery in past 30 days	8 (19.0%)	9 (25.7%)	0.483
Intensive care admission	8 (19.0%)	6 (17.1%)	0.829
Polymicrobial	5 (11.9%)	10 (28.6%)	0.066
Active empirical therapy	19 (45.2%)	15 (42.9%)	0.834

CAZ: Ceftazidime; HIV/AIDS: Human immunodeficiency virus/ Acquired immune deficiency syndrome

*Data are number of patients (%), unless stated otherwise.

†Device used included central venous catheter, peripherally inserted central catheter, arterial line, prosthetic heart valves, urinary catheter, permanent catheter for dialysis, tracheostomy tube, percutaneous transhepatic cholangiogram and percutaneous nephrostomy tube.

Table 5. Baseline Characteristics of Patients with *Pseudomonas Aeruginosa* Bacteraemia who Received Active Definitive Therapy (TZP versus Non-TZP Treatment)*

Variable	TZP n = 17	Non-TZP n = 60	P Value
Age, median years (range)	74 (52 – 81)	64 (53 – 73)	0.185
Male	10 (58.8%)	36 (60.0%)	0.930
Site of Acquisition			
Healthcare-associated	8 (47.1%)	16 (26.7%)	0.109
Nosocomial	6 (35.3%)	29 (48.3%)	0.341
Community	3 (17.6%)	15 (25.0%)	0.748
Comorbidity			
Cardiovascular	10 (58.8%)	35 (58.3%)	0.971
Diabetes mellitus	5 (29.4%)	19 (31.7%)	0.859
Respiratory	2 (11.8%)	6 (10.0%)	1.000
Cancer	2 (11.8%)	13 (21.7%)	0.499
Renal	4 (23.5%)	11 (18.3%)	0.73
HIV/AIDS	1 (5.9%)	6 (10.0%)	1.000
Source of Bacteraemia			
Hepatobiliary	1 (5.9%)	4 (6.7%)	1.000
Intra-abdominal	1 (5.9%)	2 (3.3%)	0.532
Vascular access	1 (5.9%)	5 (8.3%)	1.000
Respiratory	4 (23.5%)	7 (11.7%)	0.247
Skin and soft tissue	2 (11.8%)	5 (8.3%)	0.646
Urinary system	4 (23.5%)	21 (35.0%)	0.373
Unknown	2 (11.8%)	16 (26.7%)	0.331
Others	2 (11.8%)	0 (0.0%)	0.046
Severity of Illness			
Median SAPS II score (range)	34 (22 – 44)	29 (22 – 38)	0.363
Median Pitt bacteraemia score (range)	2 (1 – 2)	1 (0 – 2)	0.464
Device used†	9 (52.9%)	40 (66.7%)	0.299
Surgery in past 30 days	3 (17.6%)	14 (23.3%)	0.749
Intensive care admission	1 (5.9%)	13 (21.7%)	0.173
Polymicrobial	4 (23.5%)	11 (18.3%)	0.730
Active empirical therapy	4 (23.5%)	30 (50.0%)	0.052

HIV/AIDS: Human immunodeficiency virus/ Acquired immune deficiency syndrome; TZP: Piperacillin-tazobactam

*Data are number of patients (%), unless stated otherwise.

†Device used included central venous catheter, peripherally inserted central catheter, arterial line, prosthetic heart valves, urinary catheter, permanent catheter for dialysis, tracheostomy tube, percutaneous transhepatic cholangiogram and percutaneous nephrostomy tube.

As a recent study with mathematical modeling¹⁷ and a subsequent clinical study¹⁶ demonstrated that the effectiveness of TZP for PA infection were related to MIC and illness severity, we were concerned that our use of TZP might be associated with increased adverse outcomes as we did not have MIC data to guide clinical practice. Our study was reassuring as patients treated with TZP did not do worse compared with other antibiotics, as long as activity was demonstrated by disc susceptibility testing. Additionally, TZP use was not a predictor of 30-day mortality.

Our study was performed in 2007 and 2008 before the revision of MIC breakpoint for TZP and PA by the Clinical Laboratory Standards Institute in 2012. In addition, we did not administer TZP by prolonged infusion for PA infections in 2007 and 2008. One possible reason for the effectiveness of TZP might be because the MIC for TZP for PA in our hospital was less than 16 µg/mL. It might also be due to lower illness severity as only 18.7% of our patients were admitted to ICU. In Lodise's study, prolonged infusion of TZP to achieve optimal target attainment was only shown to be associated with lower 30-day mortality in a subgroup of patients with Acute Physiological and Chronic Health Evaluation 2 score exceeding 17.¹⁶

Combination antibiotic therapy appeared to be associated with lower mortality versus monotherapy in our study. Few of our monotherapy group was treated with aminoglycoside alone, which was the main bias that previously suggested the benefit of combination antibiotic for PA infections.^{22,29} The difference in 30-day mortality between monotherapy and combination therapy might be due to the larger number of pneumonia cases (14.3% vs 0%) and infections with unknown source (23.4% vs 0%) in the monotherapy group. Respiratory infections were associated with higher risk of mortality in previous PA bacteraemia studies.^{2,7} Vascular access device infections were commonly associated with lower mortality.⁷ There were significantly lesser vascular access device infections in the monotherapy group (7.8% vs 28.6%). This might explain the lower mortality rate in combination therapy group. However, this observed benefit of combination antibiotic was not borne out by the only 2 independent predictors of 30-day mortality, which were cancer and illness severity. While empiric combination antibiotics for infections where PA is a likely pathogen may be indicated by virtue of multidrug resistance, we do not believe with current evidence, proven PA infections need to be treated with more than 1 active antibiotic, as meta-analyses of randomised controlled trials showed toxicity without any advantage.^{20,21}

We did not find inactive empiric antibiotic to be associated with higher 30-day mortality. The impact of inactive or inappropriate empiric antibiotic on mortality in PA infections was variable. Some studies reported increased

risk of mortality^{4,30} while no difference in mortality had been reported in others.^{2,5,7} This might be contributed by illness severity as increased risk of mortality was often shown in critically ill patients^{1,2,4,6,13,14} or time to active culture-guided antibiotic.^{4,30} During the study period, all patients with bacteraemia were reviewed by a blood culture notification and advisory service, which was set up by the Infectious Diseases department from 2007, to ensure active antibiotics were given within 2 days.

The limitations of our study included its retrospective study design, thus accurate data on recent admission to hospitals or non-affiliated community hospitals might be limited. The relatively small sample size limited statistical power to detect small differences in treatment outcomes. Results from the subgroup analyses comparing different antibiotics used in this study might be confounded by type 2 errors in view of the small sample sizes. More importantly, we did not have MIC data for TZP in our retrospective cohort, which might have added to evidence for or against the impact of MIC for TZP on clinical outcomes.

Conclusion

We found that cancer as comorbidity and higher median SAPS II score were independent predictors of 30-day mortality. The choice of culture-guided antipseudomonal antibiotic did not seem to affect clinical outcome in this study, however a larger sample size will be needed to confirm this finding.

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Hoarding in an Asian Population: Prevalence, Correlates, Disability and Quality of Life

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Abstract

Introduction: Hoarding is defined as the acquisition of, and inability to discard items even though they appear to others to have no value. The objectives of the study were to establish the prevalence of hoarding behaviour among the general population and among individuals with obsessive-compulsive disorder (OCD) in a cross-sectional study conducted in Singapore. **Materials and Methods:** The Singapore Mental Health Study was a cross-sectional epidemiological survey of a nationally representative sample of residents aged 18 years or older, living in households. The diagnoses of mental disorders were established using Version 3.0 of Composite International Diagnostic Interview (CIDI 3.0). Differences between 3 groups i.e. those diagnosed with lifetime/12-month Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) OCD with hoarding, those diagnosed with lifetime/12-month DSM-IV OCD without hoarding and those with lifetime hoarding behaviour without diagnosis of DSM-IV OCD were determined. **Results:** The weighted prevalence of lifetime hoarding behaviour was 2% and that of hoarding among those with OCD was 22.6%. Those who met the criteria for hoarding behaviour alone were associated with lower odds of having obsessions of contamination, harming, ordering as well as compulsions of ordering and other compulsions than those who met criteria for both OCD and hoarding. **Conclusion:** Hoarders without OCD were less impaired, in terms of comorbid psychopathology, than those with OCD with and without hoarding, and had a higher quality of life versus those with both OCD and hoarding, though still lower than that of the general population.

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Keywords: Obsessive-compulsive disorder, Singapore, Survey

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Introduction

Hoarding is defined as the acquisition of, and inability to discard items even though they appear to others to have no value, leading to clutter, distress, and disability.¹ The clutter in severe hoarding precludes the use of space to accomplish the activities for which they were designed, such as cooking, cleaning, moving through the house, and even sleeping. Interference with these functions makes hoarding a dangerous problem, putting people at risk for fire, falling (especially elderly people) and other health risks.² According to the cognitive behavioural model of hoarding, the behaviour is driven by information processing deficits, fear of losing important items that the person believes will be needed later, distorted beliefs about the nature of possessions, exaggerated emotional attachment

to possessions and avoidance of the anxiety associated with discarding and decision-making.³

The prevalence of clinically significant hoarding behaviour in the general population has been reported to be as high as 4% to 5%.^{4,5} Hoarding has been observed in non-clinical populations as well as among those with neuropsychiatric disorders such as dementia,⁶ schizophrenia,⁷ depression,⁸ compulsive buying⁹ and more frequently and notably with obsessive-compulsive disorder (OCD).¹⁰ Hoarding is not listed in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition: Text Revision (DSM-IV-TR) as one of the possible symptoms of OCD; it is however included in most clinical scales that assess OCD. Research has suggested that hoarding behaviour is a distinct condition

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from OCD, both clinically as well as genetically. Severity of OCD symptoms among those with hoarding tends to be greater than for OCD patients who do not hoard.¹⁰ Hoarders report significantly more impairment in academic, work life, family life and social relationships than non-hoarders;^{10,11} hoarders (vs non-hoarders) also report greater lifetime comorbidity with major depressive disorder (MDD), dysthymia, specific phobia and generalised anxiety disorder (GAD).¹⁰ Patients with hoarding have less insight¹² and have been reported less likely to respond to treatment¹³⁻¹⁵ than those with non-hoarding OCD symptoms. Tolin et al¹⁶ found that hoarders have a greater number of chronic medical condition and higher healthcare utilisation than non-hoarding family members. Saxena et al¹⁷ found that hoarders had lower global functioning and lower scores in the domains of safety and living situations as compared to non-hoarding OCD patients. Family studies have found greater prevalence of hoarding behaviour among first-degree relatives of hoarding pro-bands than the relatives of non-hoarding pro-bands^{18,19} as well as strong correlations among siblings on hoarding factor scores.²⁰ Samuels et al¹⁹ also found a suggestive linkage of hoarding behaviour to a marker on chromosome 14 in families with OCD.

The objectives of this study were to establish the prevalence of hoarding behaviour among the general population and among individuals with OCD in a cross-sectional epidemiological study conducted in Singapore. We also investigated sociodemographic and clinical differences between individuals with hoarding behaviour who met DSM-IV criteria for OCD (OCD plus hoarding group), individuals with hoarding (compulsions) who did not meet criteria for OCD (hoarding minus OCD group) and individuals with OCD without hoarding symptoms (OCD minus hoarding group).

Materials and Methods

Sample

The Singapore Mental Health Study (SMHS) was a cross-sectional epidemiological survey of a nationally representative sample of residents aged 18 years or older, living in households and able to speak English, Malay or Mandarin. Face-to-face interviews were completed with 6616 respondents between December 2009 and December 2010. The study was approved by the institutional review board (Institute of Mental Health, Clinical Research Committee) and the ethics Committee (National Healthcare Group, Domain Specific Review Board, Singapore). Written informed consent was obtained from all respondents and parents/guardians of respondents who were between 18 and 21 years of age, as the age of majority is 21 years in Singapore. The survey response rate was 75.9%. The study methodology is described in detail in an earlier article.²¹

Measures

The diagnoses of mental disorders were established using Version 3.0 of Composite International Diagnostic Interview (CIDI 3.0).²² Diagnostic modules for lifetime and 12-month prevalence of affective disorders, including MDD, dysthymia and bipolar disorder; anxiety disorders including GAD and OCD and alcohol use disorders i.e. alcohol abuse and alcohol dependence were included in the survey. The OCD section assessed lifetime experience of commonly reported obsessive-compulsive (OC) symptoms that were present most days for at least 2 weeks in the respondent's lifetime. The obsessions and compulsions elicited in CIDI included those related to 'saving things'. For the purposes of our study, the key question to establish a diagnosis of hoarding behaviour was, "Did you ever have a time in your life when you repeatedly carried out any of the following behaviours — Always having to save things, to the point where you could not throw away things that you no longer needed or cared about?"

Respondents who met the criteria for the symptoms of OCD were questioned further to establish onset, course and recency of the illness. Clinical severity in the past 12 months was assessed using a fully structured version of the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS)^{23,24} which is incorporated in the CIDI.

Functional impairment was assessed using the disease specific Sheehan Disability Scale (SDS)²⁵ among respondents with OCD in the past 12 months. The SDS is a self-reported scale which consists of 4 questions that measure 4 domains of role impairment including home management, ability to work, ability to form and maintain close relationships and social life. A visual analogue scale of 0 to 10 is used to measure the impairment caused by the symptoms with the response options of "none" (0), "mild" (1 to 3), "moderate" (4 to 6), "severe" (7 to 9), and "very severe" (10) interference. For the purpose of this study we categorised those who endorsed any of the response options for impairment i.e. mild, moderate, severe or very severe impairment as 'any impairment'.

Disability was also assessed using a measure of 'days out of role', where respondents were asked "how many days out of 365 in the past 12 months they were totally unable to work or carry out their normal activities because of these (unpleasant thoughts/repeated behaviours)". Chronic medical conditions were assessed by using a modified version of the CIDI check list of chronic medical disorders and the respondents were asked to report any of the disorders in the checklist. Health-related quality of life was measured using the EuroQol 5 dimension scale (EQ-5D).²⁶ We used the EQ-5D index scores for the study.

Statistical Analysis

Statistical analyses were carried out using the Statistical Analysis Software (SAS) System version 9.2. To ensure that the survey findings were representative of the Singapore population, the data were weighted to adjust for over-sampling and post-stratified by age and ethnicity distributions between the survey sample and the Singapore resident population in 2007. Mean and standard deviations were calculated for continuous variables, and frequencies and percentages for categorical variables. Differences between the 3 groups i.e. those diagnosed with lifetime/12-month DSM-IV OCD with hoarding, those diagnosed with lifetime/12-month DSM-IV OCD without hoarding and those with lifetime hoarding behaviour without diagnosis of DSM-IV OCD were determined by chi-square and analysis of variance (ANOVA) tests. Multiple logistic regression models were used to explore the association between the 3 groups and sociodemographic variables, OC symptoms, comorbid DSM-IV mental disorders and chronic physical conditions. Standard errors (SE) were estimated using the Taylor series linearisation method. Multivariate significance tests were evaluated using χ^2 tests based on design-corrected coefficient variance-covariance matrices. Statistical significance level was evaluated at the P value <0.05 using 2-sided tests.

Results

The weighted prevalence of lifetime and 12-month hoarding behaviour was 2% and 0.8%, respectively. The weighted prevalence of lifetime and 12-month hoarding among those with OCD was 22.6% and 17.1% respectively. The lifetime prevalence of OCD without hoarding, hoarding behaviour but no OCD and OCD with hoarding was 2.3% ($n = 175$), 1.4% ($n = 122$) and 0.7% ($n = 55$) respectively. The 12-month prevalence of OCD without hoarding, and OCD with hoarding was 0.9% ($n = 68$), and 0.2% ($n = 14$) respectively. We were unable to establish the 12-month prevalence of hoarding without OCD as the questions in CIDI do not address hoarding alone in the past 12 months. Table 1 shows the demographic characteristics of the study sample among the 3 groups based on lifetime prevalence. There were significantly higher odds of being 'unemployed' in those diagnosed with lifetime OCD with hoarding than those with lifetime hoarding behaviour alone.

Table 2 shows the prevalence and odds ratio of DSM-IV OC symptoms between 3 groups based on lifetime prevalence. After adjusting for age, gender and ethnicity in multiple logistic regressions, those who meet criteria for hoarding behaviour alone were associated with lower odds of having obsessions of contamination, harming, ordering as well as compulsions of ordering and other compulsions than those who met criteria for both OCD and hoarding. In

addition, those diagnosed with OCD without hoarding were also associated with lower odds of obsessions of ordering and compulsions of washing/cleaning, ordering and other compulsions than those who met both criteria.

Table 3 shows the prevalence and odds ratio of lifetime DSM-IV mental disorders in the 3 groups. As compared to those who met both, OCD and hoarding criteria, those with hoarding behaviour alone were associated with lower odds of having MDD, bipolar disorder and any psychiatric comorbidity.

Table 4 shows the prevalence and odds ratio of lifetime chronic physical conditions among the 3 groups. As compared to those who had OCD with hoarding, we found the odds of having chronic pain and peptic ulcer were lower in those diagnosed with OCD without hoarding and those with hoarding behaviour without OCD diagnosis, respectively.

There were no significant differences in the age of onset, age at interview, Y-BOCS score, work days lost, and days out of role between the 3 groups. The mean EQ-5D index was significantly higher in those diagnosed with lifetime OCD without hoarding (0.911 vs 0.831, $P = 0.003$) and in those with hoarding behaviour without OCD diagnosis (0.907 vs 0.831, $P = 0.0009$) versus those with both OCD and hoarding. Those diagnosed with both OCD and hoarding were significantly more likely to report any problems in the EQ-5D domains of mobility and pain compared to the other 2 groups.

Table 5 shows the role impairment by SDS among those with OCD with and without hoarding by 12-month prevalence. The rate of any impairment in the home management and social life domains were significantly higher in those who met criteria for OCD with hoarding than the other group.

Discussion

The lifetime prevalence of hoarding behaviour of 2% is slightly lower than that reported in other non-clinical samples of about 4%.^{4,5} These differences could be due to differences in the methodology, differences in the population or they could reflect true differences between the different populations. Unlike other studies,²⁷⁻²⁹ we did not find an association between age and hoarding. We also found no difference in the age of onset of symptoms/disorder between the 3 groups. Some previous research studies^{10,19} similarly found no difference in the age of onset of illness between hoarders and non-hoarders. However, Fontenelle et al³⁰ reported that hoarders in their clinical sample had an earlier age of onset. The 3 groups did not differ significantly in any other sociodemographic features, with the exception of those with OCD and hoarding, among whom the odds of unemployment were higher. Tolin et al¹⁶

Table 1. Demographic Characteristics of Sample in the 3 Groups (n = 352)

Univariate Analysis*					Multivariate Analysis†			
	LT OCD – Hoarding‡ (n = 175)	LT Hoarding§ (n = 122)	LT OCD + Hoarding (n = 55)		LT OCD – Hoarding vs LT OCD + Hoarding	OR	95% CI	P Value
	%	%	%	P Value	OR	95% CI	P Value	P Value
Age (years)	18 – 34	40.49	37.88	46.70	ref		ref	
	35 – 49	40.30	21.37	38.75	0.89	(0.22, 3.53)	0.86	0.29
	50 – 64	18.73	18.46	14.54	2.2	(0.36, 13.47)	0.39	0.18
	≥65	0.48	22.29	.				
	Chinese	71.68	61.93	68.95	0.45	ref		
Ethnicity	Malay	13.06	19.57	17.33	0.7	(0.25, 1.97)	0.49	0.58
	Indian	10.43	13.90	10.37	1.45	(0.47, 4.43)	0.52	0.12
	Others	4.83	4.60	3.35	2.13	(0.19, 24.18)	0.54	0.44
	Male	45.82	48.05	46.56	0.97	ref		
Gender	Female	54.18	51.95	53.44	1.55	(0.53, 4.55)	0.42	0.35
	Single	36.24	27.38	45.01	ref		ref	
Marital status	Married	50.80	54.88	42.96	0.89	(0.23, 3.51)	0.87	0.63
	Divorced/separated	12.82	4.04	12.03	1.2	(0.12, 11.81)	0.88	0.67
	Widowed	0.14	13.70	.				
	Primary and below	8.32	15.37	13.27	0.65	ref		
Education	Secondary	33.12	34.98	25.10	0.98	(0.15, 6.52)	0.98	0.78
	Post secondary	58.57	49.65	61.63	1.26	(0.4, 3.97)	0.69	0.94
	Employed	79.55	68.37	59.23	0.06	ref		
Employment status	Economically inactive	15.52	29.78	28.80	0.82	(0.18, 3.83)	0.80	0.74
	Unemployed	4.93	1.85	11.97	0.28	(0.04, 1.88)	0.19	0.03
	Low	44.40	61.76	57.89	0.45	(0.11, 3.55)	0.59	0.80
Income	Middle	37.30	24.23	26.87	1.05	(0.24, 4.61)	0.95	0.85
	High	18.30	14.01	15.24	ref			

*chi-square test.
†Multinomial regression analysis.
‡Those diagnosed with lifetime OCD without hoarding.
§Those with lifetime hoarding behaviour but no OCD.
|| Those diagnosed with lifetime OCD with hoarding.
LT: Lifetime; OCD: Obsessive-compulsive disorder; OR: Odds ratio

Table 2. Prevalence and Odds Ratio of Obsessive and Compulsive Symptoms in the 3 Groups

Variable	LT OCD without Hoarding (n = 175)		LT Hoarding Behaviour without OCD (n = 122)		LT OCD with Hoarding (n = 55)	
Obsession		P Value		P Value		P Value
Contamination	% (SE)	26.29 (3.33)	15.57 (3.29)		32.73 (6.34)	
	OR (95% CI)	0.76 (0.38, 1.49)	0.39 (0.18, 0.85)		1.00 (reference)	
Harming	% (SE)	24.57 (3.26)	18.85 (3.55)		36.36 (6.5)	
	OR (95% CI)	0.55 (0.28, 1.07)	0.43 (0.21, 0.92)		1.00 (reference)	
Ordering	% (SE)	29.71 (3.46)	24.59 (3.9)		49.09 (6.75)	
	OR (95% CI)	0.42 (0.22, 0.81)	0.35 (0.17, 0.7)		1.00 (reference)	
Other obsessions	% (SE)	36.57 (3.65)	14.75 (3.22)		25.45 (5.88)	
	OR (95% CI)	1.64 (0.81, 3.34)	0.51 (0.22, 1.17)		1.00 (reference)	
Compulsion		P Value		P Value		P Value
Washing/cleaning	% (SE)	12 (2.46)	17.21 (3.42)		25.45 (5.88)	
	OR (95% CI)	0.41 (0.19, 0.9)	0.6 (0.27, 1.32)		1.00 (reference)	
Checking	% (SE)	27.43 (3.38)	34.43 (4.31)		32.73 (6.34)	
	OR (95% CI)	0.77 (0.4, 1.49)	1.05 (0.52, 2.1)		1.00 (reference)	
Ordering	% (SE)	20 (3.03)	18.03 (3.49)		43.64 (6.7)	
	OR (95% CI)	0.31 (0.16, 0.63)	0.27 (0.13, 0.57)		1.00 (reference)	
Other compulsions	% (SE)	20 (3.03)	19.67 (3.6)		34.55 (6.42)	
	OR (95% CI)	0.48 (0.24, 0.96)	0.43 (0.2, 0.9)		1.00 (reference)	

Odds ratio (OR) was based on multiple logistic regression analysis adjusted for age, gender and ethnicity.

LT: Lifetime; OCD: Obsessive-compulsive disorder

Table 3. Prevalence and Odds Ratio of Lifetime DSM-IV Mental Disorders in the 3 Groups

Variable	LT OCD without Hoarding (n = 175)		LT Hoarding Behaviour without OCD (n = 122)		LT OCD with Hoarding (n = 55)	
		P Value		P Value		P Value
MDD	% (SE)	18.73 (4.26)	7.92 (3.05)		25.18 (8.67)	
	OR (95% CI)	0.72 (0.35, 1.51)	0.37 (0.16, 0.87)		1.00 (reference)	
Dysthymia	% (SE)	1.85 (1.47)	0.33 (0.33)		1.10 (0.80)	
	OR (95% CI)	0.44 (0.05, 3.68)	0.24 (0.02, 3.04)		1.00 (reference)	
Bipolar disorder	% (SE)	7.72 (2.94)	1.14 (0.66)		19.84 (8.48)	
	OR (95% CI)	0.54 (0.18, 1.66)	0.2 (0.05, 0.86)		1.00 (reference)	

Odds ratio (OR) was based on multiple logistic regression analysis adjusted for age, gender and ethnicity.

LT: Lifetime; MDD: Major depressive disorder; OCD: Obsessive-compulsive disorder

Table 3. Prevalence and Odds Ratio of Lifetime DSM-IV Mental Disorders in the 3 Groups (Cont'd)

Variable	LT OCD without Hoarding (n = 175)		LT Hoarding Behaviour without OCD (n = 122)		LT OCD with Hoarding (n = 55)	
	P Value		P Value		P Value	
GAD	% (SE)	6.39	2.66	1.28	0.66	13.30
	OR (95% CI)	0.64	(0.2, 2.04)	0.34	(0.09, 1.32)	1.00
Alcohol abuse	% (SE)	5.00	1.91	3.34	2.50	0.76
	OR (95% CI)	4.41	(0.53, 36.6)	1.89	(0.2, 18.18)	1.00
Alcohol dependence	% (SE)	2.34	1.55	2.98	1.35	1.42
	OR (95% CI)	0.56	(0.1, 3.33)	1.26	(0.23, 6.88)	1.00
Any comorbidity	% (SE)	36.7	5.3	5.36	1.65	52.83
	OR (95% CI)	0.72	(0.38, 1.35)	0.14	(0.06, 0.31)	1.00

Odds ratio (OR) was based on multiple logistic regression analysis adjusted for age, gender and ethnicity.
GAD: Generalised anxiety disorder; LT: Lifetime; MDD: Major depressive disorder; OCD: Obsessive-compulsive disorder

Table 4. Prevalence and Odds Ratio of Lifetime Chronic Physical Conditions in the 3 Groups

Variable	LT OCD without Hoarding (n = 175)		LT Hoarding Behaviour without OCD (n = 122)		LT OCD with Hoarding (n = 55)	
	P Value		P Value		P Value	
Respiratory conditions	% (SE)	20.08	4.14	17.87	6.19	8.36
	OR (95% CI)	3.48	(0.84, 14.51)	3.30	(0.7, 15.72)	1.00
Diabetes	% (SE)	3.35	1.67	19.76	6.82	6.44
	OR (95% CI)	0.38	(0.04, 3.79)	2.03	(0.22, 18.55)	1.00
Hypertension	% (SE)	9.97	3.22	24.64	6.06	13.82
	OR (95% CI)	0.59	(0.12, 2.76)	1.30	(0.29, 5.87)	1.00
Chronic pain	% (SE)	17.21	3.87	27.34	6.47	37.67
	OR (95% CI)	0.28	(0.1, 0.79)	0.46	(0.16, 1.35)	1.00
Cancer	% (SE)	0.19	0.01	.	.	.
	OR (95% CI)	.	.	.	.	(reference)
Neurological conditions	% (SE)	7.77	3.08	7.27	3.81	.
	OR (95% CI)	1.14	(0.2, 6.35)	1.00	(reference)	.
Cardiovascular disease	% (SE)	1.63	1.46	6.59	5.01	.
	OR (95% CI)	0.35	(0.04, 2.81)	1.00	(reference)	.
Ulcer	% (SE)	4.30	2.24	1.01	0.59	6.40
	OR (95% CI)	0.57	(0.07, 4.73)	0.09	(0.01, 0.77)	1.00
Any chronic physical condition	% (SE)	47.73	5.50	56.13	5.85	64.66
	OR (95% CI)	0.46	(0.18, 1.13)	0.50	(0.19, 1.29)	1.00

Odds ratio (OR) was based on multiple logistic regression analysis adjusted for age, gender and ethnicity.
LT: Lifetime; OCD: Obsessive-compulsive disorder

Table 5. Role Impairment by Severity of Disability Assessed by Sheehan Disability Scale

	12-month OCD without Hoarding (n = 68)			12-month OCD with Hoarding (n = 14)			
	n	%	SE	n	%	SE	P Value
Home management							
No impairment	27	42.64	8.26	2	4.91	3.78	
Any impairment	41	57.36	8.34	12	95.09	3.78	<0.05
Work							
No impairment	31	44.80	8.84	6	33.14	17.08	
Any impairment*	37	55.20	8.74	8	66.86	16.94	0.41
Relationship							
No impairment	30	34.15	7.72	3	22.10	15.93	
Any impairment*	38	65.85	7.81	11	77.90	15.81	0.12
Social life							
No impairment	32	35.47	7.72	3	22.10	15.93	
Any impairment*	36	64.53	7.83	11	77.90	15.81	<0.05
Any domain							
No impairment	18	28.54	7.69	2	4.91	3.78	
Any impairment*	50	71.46	7.76	12	95.09	3.78	0.10

*Includes those with 'mild', 'moderate', 'severe' and 'very severe' impairment.

OCD: Obsessive-compulsive disorder; SE: Standard error

similarly found that hoarding was associated with marked occupational impairment; among people who meet relatively strict diagnostic criteria for hoarding, 7% of them were on disability and 6% reported having been fired from jobs due to hoarding.

Those who meet the criteria for hoarding behaviour alone were associated with lower odds of having obsessions of contamination, harming, ordering as well as compulsions of ordering and other compulsions than those who met criteria for both OCD and hoarding. Those diagnosed with OCD with hoarding were associated with higher odds of obsessions of ordering and compulsions of washing/cleaning, ordering and other compulsions compared to those with OCD without hoarding. Our findings are similar to those reported by others who found that obsessions of symmetry and ordering compulsions were higher among those with OCD and hoarding.^{19,30} These findings have led to suggestions that hoarding may belong to a separate dimension of OC symptoms.³¹ It is possible that these findings reflect the existence of a common neuro-anatomical basis of these symptoms, while it has also been suggested that these symptoms could be secondary behavioural manifestations of hoarding.³⁰

There were no significant differences in terms of prevalence and risk of association with other comorbid psychiatric illnesses among those with OCD with or without hoarding. Our findings are different from those observed by Lochner et al¹⁰ who found in their clinical sample a

higher rate of lifetime MDD, dysthymia and GAD among those with OCD and hoarding. Other studies similarly have suggested that patients with OCD and hoarding are more likely to be associated with disorders characterised by mood swings, anxiety and impulsive behaviours.^{19,30} However, all these studies were conducted among treatment-seeking populations i.e. patients with OCD and thus there would be significant differences from the respondents in this population-based study as patient samples are more likely to have other psychopathologies and behavioural disturbances. However, it is also possible that this is indeed a true difference i.e. risk of depression among those with OCD and hoarding is not higher in our population. As suggested by Li et al³² being thrifty and saving are thought to be virtues in Chinese traditional culture and therefore a person with such characteristics may not be thought of as having a disorder and the individual may not be significantly distressed by the same. Thus, certain Asian societies may have a different view of hoarding and it may not be associated with depression. This would have implications for public health as individuals and even their families may be less likely to perceive this as abnormal and they may delay or resist help-seeking. As compared to those with OCD with and without hoarding, those with hoarding behaviour but no OCD were associated with lower odds of having MDD, bipolar disorder and any comorbidity. Grisham et al²⁹ similarly reported that those with hoarding alone in terms of psychopathology reported less worry, anxiety, stress and depression compared to those with OCD and hoarding.

Similar to other studies, we found that the rate of any impairment in the home management and social life domains were significantly higher in those who met criteria for OCD with hoarding than those with OCD without hoarding. Saxena et al^{15,17} found significantly lower functioning in OCD patients with hoarding as compared to OCD patients without hoarding. However, OCD symptoms were not more severe in hoarders than non-hoarding OCD patients. OCD patients with hoarding symptoms also showed significantly greater levels of disability in multiple domains of functioning, including work, family, romantic relationships, friendships and activities of daily life as compared to non-hoarding OCD patients in a study by Lochner et al.¹⁰ However in their study, hoarding patients had significantly more severe overall OCD symptoms and greater comorbidity with depressive and anxiety disorders than non-hoarding OCD patients. Frost et al¹¹ similarly found that, OCD patients with hoarding scored higher on anxiety, depression, family and social disability compared to non-hoarding OCD patients. In contrast, 2 studies^{29,30} found no difference in functioning scores between hoarding and non-hoarding OCD patients. While the disability and impairment in functioning seen in those with OCD and hoarding may be partly explained by comorbid anxiety and depressive symptoms in these studies, we are unable to establish this in our study as the likelihood of comorbid MDD and GAD were similar in both the groups. The domains that were most significantly affected were those of home management and social life. A possible explanation might be that the marked clutter in a hoarder's home may affect the livability and ability to use the living space, thus interfering with home management. Hoarding may also affect relationships with family members and neighbours and restrict visits from friends and relatives which affect the social life of a hoarder, leading to isolation. This is supported by a study which found that family members who cohabit with hoarders feel embarrassed about the condition of their home, and may harbour feelings of rejection and hostility toward the hoarder.¹⁶

The mean EQ-5D score in the overall Singapore population was 0.951,³³ while that of 'healthy controls' (i.e. those without a diagnosis of the mental and physical illnesses included in the SMHS) was 0.98.³⁴ It is interesting to note that in the present study all 3 groups had lower EQ-5D indices than the population as well as that of 'healthy controls'. However, those with OCD and hoarding reported lower subjective quality of life as compared to those with OCD without hoarding as well as those with hoarding behaviour without OCD diagnosis.

The main limitation of our study was that it did not include any specific rating scale for hoarding. The modified Y-BOCS checklist adapted in CIDI was the only instrument used

to establish hoarding and its severity. Another potential limitation of the present study is the exclusive reliance on self-report for the hoarding symptoms. A clinical interview as well as some corroboration with interviewer observations might be more reliable and valid than self-report measures of hoarding, particularly given the poor insight among those with hoarding.³⁵ We did not examine the phenomenology of hoarding such as the items hoarded and the reasons for hoarding. Lastly, we did not conduct a clinical validation in the sample population.

These limitations notwithstanding, the strengths of our study are that it is a nationwide survey of a representative multiethnic population that examined psychiatric morbidity using a structured diagnostic instrument with face-to-face interviews, and psychiatric diagnoses were made according to DSM-IV criteria. Our population-based study on those with hoarding without OCD, OCD with hoarding and OCD without hoarding has some rather unique findings. Our study shows that hoarders without OCD are a somewhat distinct group. They are less impaired than those with OCD with and without hoarding, in terms of comorbid psychopathology, and have a higher quality of life than those with OCD and hoarding, though still lower than that of the general population. Grisham et al²⁹ have suggested that the ego-syntonic nature of compulsive hoarding may explain the lack of distress in this unique group. They also suggested that pure hoarding may be better conceptualised as an impulse control disorder given that individuals derive pleasure from it. On the other hand, the 2 groups with OCD with and without hoarding differ from each other mainly in terms of the association with other OC symptoms with those with hoarding behaviour more likely to be associated with symptoms of symmetry obsessions and ordering compulsions. Hoarders with OCD also reported a lower quality of life as compared to those with OCD without hoarding. However, the 2 groups did not differ on the level of comorbid psychiatric disorders or severity of symptoms.

Conclusion

Our study is one of the few (and the first Asian) population-based studies that has examined hoarding behaviour. This is in contrast to majority of studies in the extant literature that have been conducted in the clinical population to examine hoarding. Given the large treatment gap reported in studies, clinical studies may represent a population of those with severe symptoms or comorbidities that may not be representative of the community sample of people with OCD and/or hoarding. Future studies using specific scales such as the University of California Los Angeles (UCLA) Hoarding Severity Scale³⁶ or Savings Inventory Revised³⁷ should be conducted on community samples to understand the phenomenology and true impact of hoarding in the population.

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When Traditional Model Meets Competencies in Singapore: Beyond Conflict Resolution

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Abstract

Introduction: The implementation of competency-based internal medicine (IM) residency programme that focused on the assurance of a set of 6 Accreditation Council for Graduate Medical Education (ACGME) core competencies in Singapore marked a dramatic departure from the traditional process-based curriculum. The transition ignited debates within the local IM community about the relative merits of the traditional versus competency-based models of medical education, as well as the feasibility of locally implementing a training structure that originated from a very different healthcare landscape. At the same time, it provided a setting for a natural experiment on how a rapid integration of 2 different training models could be achieved. **Materials and Methods:** Our department reconciled the conflicts by systematically examining the existing training structure and critically evaluating the 2 educational models to develop a new training curriculum aligned with institutional mission values, national healthcare priorities and ACGME-International (ACGME-I) requirements. **Results:** Graduate outcomes were conceptualised as competencies that were grouped into 3 broad areas: personal attributes, interaction with practice environment, and integration. These became the blueprint to guide curricular design and achieve alignment between outcomes, learning activities and assessments. The result was a novel competency-based IM residency programme that retained the strengths of the traditional training model and integrated the competencies with institutional values and the unique local practice environment. **Conclusion:** We had learned from this unique experience that when 2 very different models of medical education clashed, the outcome may not be mere conflict resolution but also effective consolidation and transformation.

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Key words: ACGME-I, Graduate medical education, Internal medicine residency programme

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Introduction

In 2010, graduate medical education in Singapore underwent major reform. With the implementation of competency-based residency programmes, hospitals in Singapore became the first outside the United States (US) to adopt a training structure based on the Accreditation Council for Graduate Medical Education (ACGME) core competencies and seek accreditation by the same council. Internal medicine (IM) was one of the first 7 specialties that received a mandate from the Ministry of Health, Singapore (MOH) to redesign its postgraduate medical education (PGME) structure to meet the standards of the newly constituted ACGME-International (ACGME-I).

This educational reform marked a dramatic departure from the traditional process-based curriculum in Singapore that emphasised content delivery (medical knowledge and patient care), and relied heavily on workplace-based global ratings and high stake summative assessments to ensure competence. The transition to a competency-based curriculum that focused on the assurance of a set of 6 core competencies presented major challenges to the participating institutions. The mandate ignited debates within the local IM community about the relative merits of the traditional versus competency-based models of medical education in ensuring that residents could provide high-quality medical

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care when they enter independent practice.

Scepticism over the need and feasibility of the transition had arisen from 2 main concerns. First, the PGME administrative framework, healthcare structure, hospital workload and service requirements in Singapore were significantly different from those in the US. Many were worried that the ACGME-I competency framework and standard, which had evolved from the US healthcare structure, could not be readily adopted by the local institutions. Indeed the mandate was viewed by some as an unrealistic expectation. Second, the ongoing controversy over the competency-based approach to medical education suggested a lack of consensus in the larger medical education community on the value of the model.^{1,2,3}

Caught in the middle of this powerful wave of education reform and controversy, the University Medicine Cluster (UMC) of the National University Health System (NUHS) took the view that, though the mandate was likely to cause sharp division of opinions among faculty members, put a strain on the limited resources and threaten to disrupt the fragile balance between patient care, research and education, it presented an important opportunity for the department to re-evaluate its training structure. In fact, the momentum generated by the national effort to transform the landscape of PGME could serve as a useful force to overcome inertia that was inherent in large academic departments and allow broad education reform.

In this article, we describe a unique natural experiment where an IM residency programme based on the ACGME core competencies was created within the constraints and challenges described above. Because of the need to do more with less, both in terms of time and resources, the constraint had encouraged far-reaching innovations within the programme. We describe the steps taken by the IM residency committee in order to systematically examine the existing training structure and critically evaluate the relative merits of the traditional versus competency-based educational models to develop a new training curriculum aligned with institutional mission values, national healthcare priorities and ACGME-I requirements. The result was a novel competency-based programme that retained the strengths of the existing training model, and integrated the competencies with institutional values, and the unique local practice environment.

Materials and Methods

The Existing Training Structure

It is beyond the scope of this article to describe details of the existing training structure for IM in Singapore. Briefly, the existing training programme, known as basic specialist training (BST), commenced a year after housemanship

(internship) and normally lasted for a minimum of 3 years. Training was provided in accredited departments in all public sector teaching hospitals in Singapore. Learning objectives, learning content and posting requirements, were determined and centrally administered by the Joint Committee of Specialist Training (JCST). Residents in the programme typically were rotated through various departments in different hospitals and kept a logbook record of their work and training. The training was overseen by the JCST who received interval assessment reports on the global performance of trainees from the various clinical departments and concluded with a high stake summative clinical examination (Master of Medicine (MMed) and Diploma of Membership of the Royal Colleges of Physicians of the United Kingdom, MRCP (UK)).

A Collaborative Approach in Defining the Graduate Outcomes and the Curricular Blueprint

The IM residency committee recognised that a collaborative approach was essential to ensure sustainability and ownership of the new curriculum in UMC which was a large, university-affiliated department whose faculty members often had many competing priorities. A residency retreat was organised to bring together faculty from various subspecialties to initiate a collaborative and cross-disciplinary discussion, and to promote innovative curricular planning. The planning started with an attempt to define the characteristics of graduates from the NUHS IM residency programme and link these characteristics to the ACGME core competencies. From the extensive dialogue, a few themes emerged. First, at the level of personal attributes, the programme should focus on developing lifelong learners who are equipped with the capacity to continue to learn from experience and practice IM effectively in a rapidly changing environment. In addition, the programme graduates should possess professionalism that reflected the core mission values of this institution. Second, at the practice level, the new training curriculum should ensure that the graduates are sensitive to the “system” aspects of healthcare (such as system inefficiencies and medical errors) and possess a good understanding of the priorities and the unique system of care delivery in Singapore. Third, in developing the new graduate outcomes, the programme should attempt to contextualise the ACGME core competencies to reflect the local condition of practice and healthcare system. The programme should seek to retain the strengths of the existing training structure while integrating the elements of a competency-based model. Finally, the new graduate outcomes should be used as the blueprint for curricular design so that alignment between learning, teaching activities and outcomes could be ensured (Fig. 1).

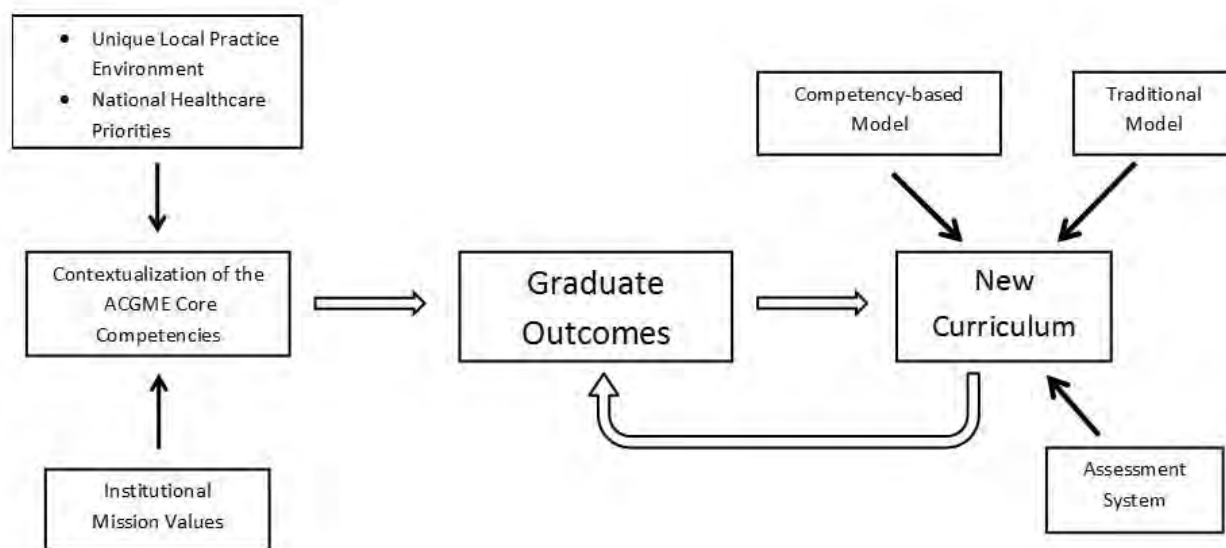


Fig. 1. Graduate outcomes were developed through contextualisation of the core competencies and used as blueprint for curricular design. This approach led to alignment between outcomes, learning activities and assessment system, and allowed integration of the traditional and competency-based models.

Results

Contextualisation of the Core Competencies

Society's expectations of doctors were the key factors that influenced the way the profession conceptualised its practitioners' competence. As the maxim of physician self-regulation was the altruistic expectation that the public interest be served, how the profession defined its practitioners' competence was very much related to how the population they served perceived and appreciated its professional service.⁴ Even though the doctors' competence was generally regarded as something that transcended borders, a definition of competence that possessed a certain level of context specificity would be more helpful and relevant for educators to focus their efforts when designing a curriculum. This was particularly true for competencies like professionalism and systems-based practice. To that end, the teaching, learning and assessment of competencies must respond to the healthcare needs of the larger society and the mission of the institution's local community.

Singapore's healthcare priorities are dominated by issues common to many developed countries: a growing ageing population, changing disease patterns from communicable diseases to chronic lifestyle-related diseases, higher public expectations and avoidance of fragmentation of care. Singapore has one of the fastest ageing populations in the world, with those over 65 years old estimated to represent 19% of the population by 2030, the second highest percentage in Asia, lagging behind only Japan.⁵ The combination of a healthcare funding model that was distinct from most developed economies,⁶ changing healthcare

priorities and rapidly expanding demand for healthcare services had resulted in a unique practice environment that demanded specific competencies from the internists in the areas of professionalism and systems-based practice for effective delivery of care. A useful context-specific attribute of a competent internist in Singapore would therefore be: professionalism in the care of elderly patients, ability to deliver holistic medical care to the geriatric population and patients with chronic diseases, and familiarity with the local healthcare resources and infrastructure in order to provide an effective connection between acute and long-term care. By the same token, as the core values of NUHS were summarised by the mnemonic 'TRICE', standing for Teamwork, Respect, Integrity, Compassion and Excellence, the definition of professionalism as a competence for practising physicians in this institution must reflect these core values.

Through contextualisation of the competencies, we were able to maintain the relevance and sustainability of the new programme. This alignment had helped to make the new programme more readily accepted by the faculty and hospital administration, and thus, facilitated its implementation.

A Systematic Re-examination of the Current System and Comparison of 2 Training Models

Traditional versus Competency-based Models

The existing training framework was one of workplace-based PGME where trainees learned through hands-on experience in everyday ward work. Learning occurred

through the apprenticeship model of clinical training. Assessment involved global ratings by faculty who had observed the residents in a clinical setting over the length of a clinical rotation. This traditional model which was process-based, gave equal weight to both process and outcome of learning, and evaluated skills globally contrasted with the competency-based model that required specification of learning objectives in relation to each of the broad competencies and objective measurement of their achievement by the residents. The debate on the relative merits of the 2 models was ongoing and was far from conclusive.¹⁻⁴

The traditional training model suffered from a number of deficiencies. First, even though the training curriculum had a well organised body of learning content and structure, it did not give adequate attention to the learning and development of competence in individual domains. Apart from medical knowledge and patient care, residents' development in other important roles of physicians (as communicator, collaborator, manager, health advocate, scholar and professional), though implied, was not explicitly expressed or addressed. Second, the use of global ratings at the end of rotations was prone to generosity bias, halo effect and the lack of reproducibility associated with subjective evaluation.⁷

However, it could be argued that the traditional model addressed a niche in medical teaching and assessment that could not be met by the competency-based approach. It had been suggested that focusing teaching and assessment on performance in individual domains of medicine, rather than on performance in caring for patients, would distract faculty from what they should be doing — observing residents caring for patients in a variety of clinical settings and under different clinical circumstances.^{1,4} The ability of residents to translate and integrate their knowledge, skills, and attitudes so that they could perform the complex tasks required to deliver high quality medical care was considered by some to be a more relevant high-level competence than the ACGME competencies that represented a set of measurable attributes.¹ This higher order competence involved sensitivity to clinical context and could only be validly appraised in such a context by fully competent appraisers.² The traditional model that emphasised the residents' overall performance in delivering medical care in the workplace and paid little attention to the individual domains may, paradoxically, be more useful in assessing this higher order competence and helping the residents to advance from someone who possessed the right attributes to someone who did the right thing.

From these considerations and adapting the concept proposed by other educators,^{8,9} we reconciled the differences between the 2 models by conceptualising the graduate

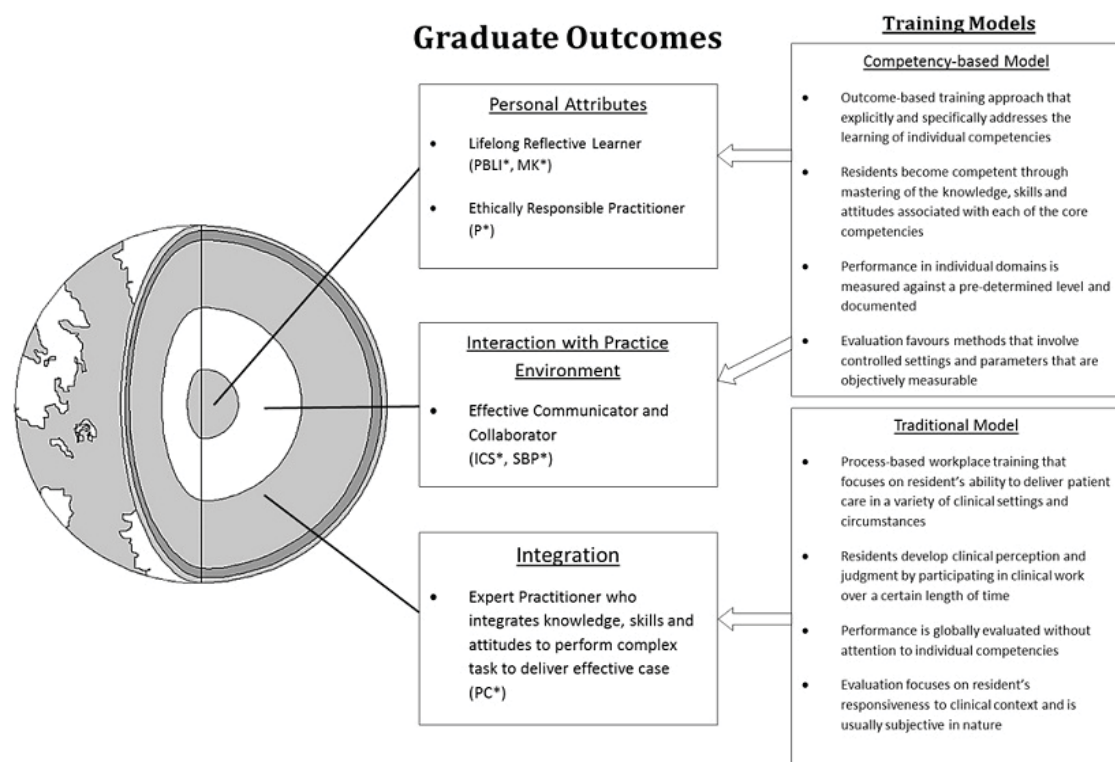
outcomes of this programme as a cutaway view of the earth (Fig. 2): the “core” was represented by competencies that reflected personal attributes (practice-based learning and improvement, professionalism, medical knowledge), the “mantle” consisted of competencies that represented interaction with the practice environment (communication skills, systems-based practice), and the “crust” depicted higher competency, that is the ability of a graduate to translate and integrate all the other competencies into the delivery of high-quality medical care (patient care). By organising the competencies into spherical layers that wrapped around the core, the graduate outcomes became an explicit and logical basis for the development of the new curriculum. Through achievement of the competencies, residents advanced stepwise from possession of the right attributes to effective interaction with the practice environment and finally successful integration of all the skills to deliver effective care. The learning content, rotation system, and assessment systems were restructured to match the new graduate outcomes, with the most appropriate activities and assessment tools selected to support each competency. The process was guided by 2 broad principles. First, the competency-based approach¹⁰ that explicitly and specifically addressed the learning of individual domains was adopted to enhance the learning of competencies related to personal attributes and interactional abilities. Second, the traditional model that was characterised by opportunistic workplace-based learning, observation and global ratings was retained to complement the teaching and assessment of the residents' holistic ability to bring the discrete “building blocks” competencies to bear in the clinical setting.

An Assessment System Aligned with Outcomes

We used the core competencies as the framework for assessment and linked all assessment methods to one or more of the 6 domains. Assessments methods were selected from the ACGME toolbox to match the competencies. The assessment system placed greater emphasis on continuous workplace performance with information-rich activities receiving more specific attention for assessments. To support the new model of graduate outcomes, on top of individual competencies, residents were evaluated by the supervisors on how well his or her performance met the actual demands of the clinical situations in workplace. The use of global ratings at the end of each rotation ensured that residents progressed from “someone who knows” to “someone who does”.¹¹

Portfolio

Periodically, residents performed a strengths-weaknesses analysis of the portfolio and constructed self-direction in



their learning and used that as the focus for discussion with their supervisors to achieve an agreement on the progress of their learning, formulate new learning goals, and construct personal development plans.

In summary, the mixed formative and summative approach to workplace-based assessment and the careful selection of assessment tasks to allow a portfolio-based reflective process were implemented to align the learning activities with the graduate outcomes. This deliberate design of the assessment system helped to consolidate the curriculum and ensure the graduate outcomes.

Conclusion

Recognising that debate on medical education was ongoing but curriculum reform was urgent, we seized the opportunity provided by the national mandate to achieve sweeping changes in the PGME at the UMC. Through contextualisation of the competencies and examination of the institutional mission values and national healthcare priorities, graduate outcomes were developed for the new programme. These were conceptualised as competencies grouped into 3 broad areas: personal attributes, interaction with practice environment and integration, and used as the blueprint to guide curricular design and achieve alignment between outcomes, learning activities and assessment system. Through achievement of the competencies, residents advanced stepwise from development of the right attribute to effective interaction with the system and finally integration

of all the skills, knowledge and attitudes to deliver medical care that met the demands of the local practice environment. Preliminary evaluation results showed that the programme was successful in focusing resident attention on the graduate outcomes.

However, our experience may have limited generalisability. NUHS had a different organisation structure, learning environment, set of core institutional values and priorities from many institutions. These factors had enhanced our programme's ability to implement changes that may not be so readily adapted by programmes situated in other institutions. We were also aware that the redesigned programme was only in its infancy and long-term data regarding the results were not yet available. Nevertheless, we had learned from this unique experience that when 2 very different models of medical education clashed, the outcome may not be mere conflict resolution but also effective consolidation and transformation.

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The authors wish to thank all the core faculty members of the internal medicine programme for their contributions in curriculum design and implementation: Ms Jerrine Seah, Ms Diana Ng, Ms Chu Xiang Kek, Ms Ruby Lim, Ms Lipin Tan (programme coordinators) and Ms Han Wei (Education Research Assistant) for the administrative support, Associate Professor Shirley Ooi (Designated Institutional Officials, Residency Programs, NUHS) and Ms Clara Sin (Director of Medical Affairs, Education) for guidance and support, and the NUHS Internal Medicine residents themselves, for whom this work was carried out.

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Magnetic Resonance-Guided Focused Ultrasound Surgery (MRgFUS) of Uterine Fibroids in Singapore

Nian-Lin R Han, ¹MD, PhD, Chiou Li Ong, ²MBBS, FRCR, FAMS

Abstract

Introduction: Uterine fibroids are the most common type of gynaecologic benign tumours, occurring in 25% to 50% of women during their reproductive lives. About half of the affected women have clinically significant symptoms, including abnormal bleeding, menstrual pain, frequent urination, constipation and abdominal distension. Magnetic resonance-guided focused ultrasound surgery (MRgFUS) has been used to treat patients with benign lesions and a variety of malignancies. The objective of this study is to evaluate symptom relief before and after MR-guided ultrasound ablation of fibroids. **Materials and Methods:** A total of 37 patients with symptomatic uterine fibroids were treated in this study. **Results:** MRgFUS treatment led to a significant, time-dependent decrease in not only Symptom Severity Scores (SSS), but also the mean fibroid volume. The average reductions in volume were 41.6% and 52.6% at 6 months and 12 months respectively ($P < 0.05$). The mean SSS of the 37 patients was 41.7 ± 2.8 before treatment whereas the average SSS was 26.9 ± 3.6 , 20.7 ± 3.4 , 18.5 ± 3.6 , 16.5 ± 7.1 , 9.8 ± 3.6 at 3 months, 6 months, 1 year, 2 years, and 3 to 4 years respectively. The decrease in scores was significant at all time points up to 3 to 4 years ($P < 0.05$ and $P < 0.001$). **Conclusion:** MRgFUS is a safe and effective non-invasive treatment for patients with symptomatic fibroids.

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Key words: Non-invasive treatment, Symptom Severity Score

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Introduction

Uterine leiomyomas, or fibroids, are the most common type of gynaecologic benign tumours, occurring in 25% to 50% of women during their reproductive lives. About half of the affected women have clinically significant symptoms, including abnormal bleeding, menstrual pain, frequent urination, constipation, and abdominal distension.^{1,2} The conventional treatment for symptomatic women who have completed their families is hysterectomy, or myomectomy in women who wish to preserve their uteri.²⁻⁴ Many of these are open surgical procedures associated with risks such as infection and blood loss. According to reports from the United States of America (USA),^{5,6} an estimate of over US\$2 billion is spent each year on hospitalisation for problems related to uterine fibroids, and more than US\$4600 is spent on the treatment of fibroids per woman per year.

Moreover, the cumulative rate of uterine fibroid recurrence at 12 and 24 months after abdominal myomectomy has been reported at 12.4% and 46.0%, respectively.⁷ Many women who wish to avoid surgical treatments or preserve the uterus increasingly seek less-invasive options. In order to reduce the cost, morbidity and lifestyle impact of surgery, several alternative approaches, for example, hormonal therapy, uterine artery embolisation (UAE) and focused ultrasound (FUS) surgery, have been used for the treatment of uterine fibroids.

FUS has been used to treat patients with benign lesions and a variety of malignancies. It uses FUS energy which is delivered to tissues deep within the body through intact skin. The high intensity of focused ultrasound energy is capable of producing thermal coagulative necrosis at a precise point. Magnetic resonance imaging (MRI) offers

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excellent soft tissue contrast and anatomic resolution needed during targeting, and temperature sensitivity for real-time treatment monitoring. The feasibility of an MR-guided focused ultrasound (MRgFUS) system was first described in 1995⁸ and this method has been tested extensively for the treatment of breast cancer, malignant bone tumour and liver cancer for more than 10 years.

The present study is the first report in Singapore of the use of MRgFUS to treat uterine fibroids. KK Women's and Children's Hospital (KKH) is the only centre in Singapore with a MRgFUS facility for the treatment of uterine fibroids. Many reports have shown that MRgFUS ablation is feasible and safe, with 6-month and 1-year follow-up demonstrating improvements in fibroid-related symptoms. Stewart et al⁹ had shown that 71% of women undergoing MRgFUS reached the targeted symptom reduction at 6 months, and 51% reached this at 12 months. A modest volume reduction similar in magnitude to the treated volume was seen. The same group also reported that their modified protocol achieved better outcomes; 91% of patients reached a targeted symptom reduction at 12 months while no serious adverse events were recorded.¹⁰ The recent study from Gorny et al¹¹ demonstrated that 86%, 93% and 88% of patients reported relief of symptoms at 3-month, 6-month and 12-month follow-up respectively. However, reports on long-term sustained symptom relief are few. In our study, we assess the effectiveness of MRgFUS ablation for uterine fibroids and show the post-treatment symptom relief at intervals of 6 months, 1 year, 2 years, and 3 to 4 years.

Materials and Methods

This prospective study was approved by the Ethics Committee of the Central Institutional Review Board of Singapore Health Services. Informed consent was obtained from each patient before every procedure. All MRgFUS procedures were performed using ExAblate[®] 2000 (InSightec, Haifa, Israel), which is integrated with a 1.5 Tesla MRI scanner (Signa HDxt; GE Healthcare, Waukesha, Wisconsin, USA).

Patients

From August 2006 to December 2009, 37 patients with symptomatic uterine fibroids were treated in this study. Most of the patients found out about this procedure through the Internet. Each patient was seen by a gynaecologist as well as the treating radiologist who obtained the patient's medical history, and assessed uterine fibroid symptoms according to the Uterine Fibroid Symptom and Quality of Life questionnaire (UFS-QOL).¹² The UFS-QOL consists of 37 questions, of which the initial 8 related to menstrual flow and bulk problems were used to calculate the Symptom

Severity Scores (SSS). The inclusion criteria were as follows: (i) women in good general health, older than 21 years old, able to give independent consent, (ii) uterine fibroids assessed by MRI to be accessible to the focused ultrasound, and (iii) ability to communicate with nurse or physician during the procedure. Those with multiple fibroids (more than 3) were usually deemed unsuitable for this form of treatment. Exclusion criteria were derived from the ExAblate[®] commercial treatment guidelines. In general, patients were excluded if they had contraindications to MRI such as non-MRI compatible implanted metallic devices or extreme obesity. Pregnant women and patients with extensive abdominal scar, post-menopausal women, uterus size larger than 24 weeks gestation or other significant pathology (i.e. ovarian lesion, active pelvic infection) were also excluded from the treatment.

Pre-treatment MRI

All eligible patients underwent pre-treatment MRI with a standardised protocol. Assessment of fibroid number, size, volume, location and enhancement after administration of gadolinium was made. The scan was performed with the patient in the prone position, and 3 orthogonal T2-weighted images of the uterus were obtained followed by fat-suppressed T1-weighted images before and after gadolinium injection. The images were analysed to determine patient suitability for the procedure. The bulk of the fibroid mass should not be more than 12 cm away from the skin. This may be assessed during the screening MRI scan and measured from the skin surface to the centre of the fibroid. If it is over 12 cm, the likelihood of adequate sonication is diminished. Patients with bowel that could not be shifted from the potential beam path were excluded from the study, as gas or hard particles in the bowel may reflect or absorb the ultrasonic energy.

The fibroid volumes were calculated by a software programme in the MRI workstation using slice-by-slice area measurements, multiplied by the slice thickness. In cases where this was not possible, 3 orthogonal measurements of the fibroid were taken and calculated using the prolate ellipsoid formula. Patients who had total fibroid volume of 500 cm³ or more were pre-treated with a gonadotrophin-releasing hormone (GnRH) analogue for 3 months in an effort to reduce the size and vascularity of fibroids.

Magnetic Resonance-guided Focused Ultrasound Surgery

MRgFUS was performed under intravenous conscious sedation and analgesia in the form of midazolam and pethidine. Vital signs were monitored continuously and the patients were in direct visual and voice contact with the treating radiologist at all times. A switch was provided

to the patient at the beginning of the treatment to stop the sonication at any time she experienced excessive heating or abnormal sensations in her lower limbs or back. A nurse was assigned to monitor the patient in the MRI room at all times during the treatment. The patients were carefully positioned prone on the therapeutic system with the anterior abdominal wall in contact with a coupling medium placed over the ultrasound transducer used in the ablation. Pre-treatment T2-weighted MRI were acquired and used in drawing the regions for treatment. The equipment then mapped out the sonication spots in the regions drawn on the fibroids (Fig. 1A). The equipment can also display the ultrasound beam path, in 2 other orthogonal MRI views (sagittal or axial) of the target (Fig. 1B). The size and concentration of the spots may vary according to the type of fibroid. All treatments were performed by a single radiologist.

After approval of the treatment plan, a low-energy test power was aimed within the targeted fibroid to confirm the focus point before therapeutic levels of sonications were used. These verification sonications generate a very low non-ablative temperature rise at the focal point. Any discrepancy caused by the mechanical alignment of the system or movement in the location of the focal spot can be corrected at this point. Then a few higher power pulses were delivered at the target point until adequate temperature and thermal dose was reached. With rapid MRI (fast spoiled gradient-recalled echo sequences) to monitor the temperature and position of the focused ultrasound beams, the targets in each region were treated in turn. At each sonication, line graphs showing the temperature change in the target volume were recorded by the equipment (Fig. 2).

This process was repeated for each target until the planned treatment volume was achieved. The therapeutic energy and the sonication time were adjusted based on patient feedback and temperature map. Adverse events and the number of sonications were recorded. The patients were observed for about 2 hours following MRgFUS treatment and were discharged if there were no complications.

Follow-up

Post-treatment MRI was performed immediately after completion of treatment to determine the changes in uterine fibroid perfusion. Gadolinium-enhanced MRI was used to measure the non-perfused volume (NPV). After discharge, the patients were followed up with a telephone interview over the next few days, and subsequently a week later at the outpatient clinic. Further follow-up assessments were carried out a month following treatment, and subsequently at 3 months and 6 months. Follow-up MRI studies were performed at 6 months and 1 year after MRgFUS. Information about possible side-effects as well their

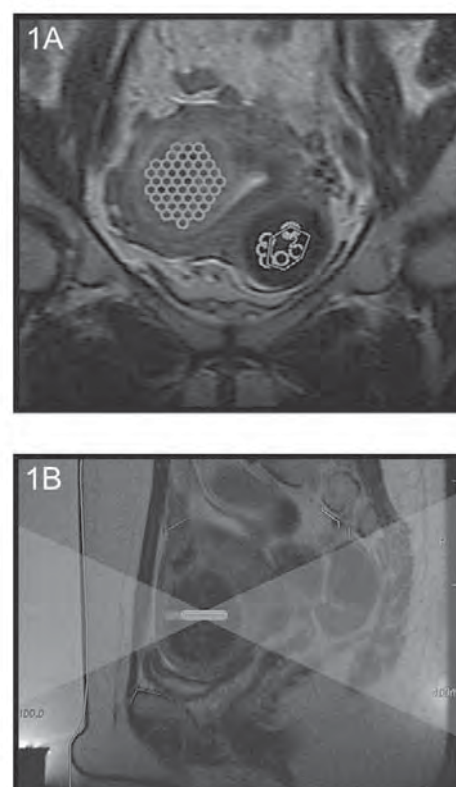


Fig. 1. (A) Coronal MRI showing the overlay of sonication targets in the fibroids. The regions indicated by an arrow are targets that cannot be treated due to various reasons such as overlying bowel or proximity to the spine (far-field bone). (B) Sagittal MRI showing the treatment target (small rectangle) in the fibroid and ultrasound beam path (triangles).

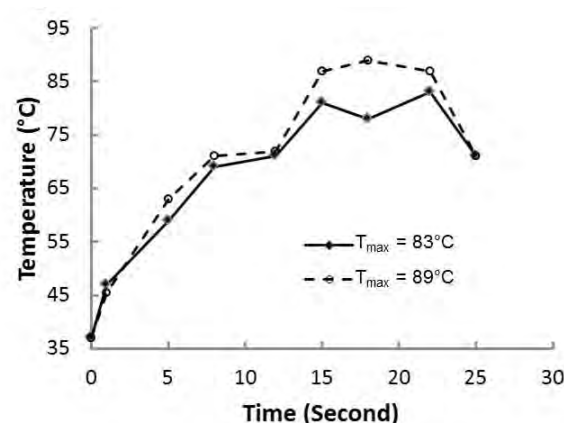


Fig. 2. Line graphs showing temperature rise within the sonicated tissue.

fibroid-related symptoms and their severity were recorded using SSS questionnaire at 3 months, 6 months, 1 year, 2 years and 3 to 4 years. A 10-point reduction in SSS score, which was validated earlier, was used as an indication of symptom improvement.

T2-weighted MRI was used to compare the fibroid size before and after MRgFUS. The NPV was defined as the fibroid coagulation volume in contrast-enhanced MRI. The NPV was taken as ablation volume as we excluded the fibroids from treatment that showed signs of degeneration or did not demonstrate enhancement. The fibroids showing heterogeneous enhancement were included if there were no large confluent areas of non-enhancement. The follow-up MRI was read independently by staff radiologists who may not be involved in the treatment. The signal intensities of the fibroids were assessed by the principal investigator in comparison to the native tissues in the patients, e.g. a fibroid was hyperintense, or had high signal intensity, when its signals were higher or similar to myometrium. A fibroid with low signals would have signals similar to that of skeletal muscles. Fibroids with intermediate signals were those with signals higher than skeletal muscles but lower than the myometrium. This classification has been used in other studies.^{13,14}

Statistical Analysis

The distribution of data was first identified by Kolmogorov–Smirnov test and Shapiro–Wilk test. For normal distribution data, the comparisons of means were assessed by paired t-test. For skewed distribution data, Wilcoxon signed-ranks test was used to evaluate the difference between before and after MRgFUS treatment. Data are reported as the median and 95% confidence interval (CI) for skewed distribution data, or mean $\pm$ SD for normal distribution data.

The percentage change of fibroid volume is defined as the following:

$$\text{Percentage change of fibroid volume (\%)} = \frac{\text{Fibroid volume at 6 or 12 months} - \text{Fibroid volume before treatment}}{\text{Fibroid volume before treatment}} \times 100$$

Auto-regressive model for repeated measurement was used to measure the significance of the treatment effect. Linear regression analysis and Spearman correlation were used to evaluate for a correlation between SSS change and types of fibroids and treatment volume ratio. A significant difference was indicated by $P \leq 0.05$. IBM SPSS Version 19 software (New York, USA) was used for all data analysis.

Results

Characteristics of Patients

Thirty-seven patients with 50 fibroids were treated by MRgFUS in this prospective study. The average age of

the patients was 44.6 years old (range, 34 to 52 years old). Twenty-eight of 37 (75.7%) treated patients were evaluated by contrast-enhanced T1-weighted image at 6 months after MRgFUS treatment, while 11 (29.7%) patients were evaluated at 12 months. Using the SSS questionnaire, 22 of 37 (59.5%) treated patients were assessed at 3 months, 25 (67.6%) were assessed at 6 months, 10 (27.0%) were assessed at 1 year, 10 (27.0%) were assessed at 2 years and 8 (21.6%) were assessed at 3 to 4 years. A total of 10 patients (27.0%) underwent surgery (6 patients had hysterectomy, 4 patients had myomectomy) at 2 years follow-up.

Clinical Outcomes

The data distribution for the fibroid volume before treatment, 6 months after treatment, 12 months after treatment and that of non-perfusion volume were analysed using the Kolmogorov–Smirnov test and Shapiro–Wilk test for the non-normal distribution, and were represented by their median values, whereas the percentage of NPV and percentage changes after the treatment showed normal distribution. The median fibroid volume was 105 cm³ (95% CI, 74.3 to 144 cm³) (Table 1). The MRgFUS resulted in a median NPV (indicative of successful ablation) of 46.9 cm³ (95% CI, 31.5 to 83.2) and the mean ratio of the NPV to the fibroid volume was 55.1 $\pm$ 22.2% (range, 7.2% to 90.9%). Contrast-enhanced T1-weighted images 6 months after MRgFUS treatment showed more than 50% fibroid ablation in 10 patients, 30% to 49% in 11 patients, 10% to 29% in 6 patients and less than 10% in 3 patients. Figure 3 shows the sagittal view of T2-weighted MRI from a 48-year-old patient over time. The patient was diagnosed with fibroids for 10 years and had heavy menstruation, dysmenorrhea and gradually worsening pelvic pressure.

Table 1. Characteristics of Patients with Uterine Fibroids Treated with Magnetic Resonance-guided Focused Ultrasound Surgery (MRgFUS)

Variable	Mean $\pm$ SD*/Median†	Range
Age (years)*	44.6 $\pm$ 4.2	34 – 52
Total number of fibroids treated	50	
Median volume of fibroids (cm ³)†	105.1	3.2 – 601.4
Median non-perfused volume‡ (cm ³)†	46.9	1.1 – 435.0
Average non-perfused volume percentage (%)*	54.0 $\pm$ 22.6	7.2 – 90.9
Average number of sonications*	81.5 $\pm$ 35.2	21 – 154

*Data are expressed as mean $\pm$ SD.

†Data are expressed as median.

‡The non-perfused volume (NPV) is measured on the post-contrast images using a segmentation technique. The non-enhanced part of the treated fibroid is calculated as a percentage of the total fibroid volume obtained on the T2-weighted images.

Prior to treatment, she was treated with 11.25 mg leuprolide acetate 3-month depot (gonadotrophin agonist). The size of her fibroid on the day of the treatment was 210.4 cm³ and the treatment volume was 88.5 cm³ (42.1%). At the 6-month follow-up evaluation, her fibroid showed further reduction in size to 137.6 cm³ (34.6% reduction in volume). The patient experienced significant improvement in her symptoms, and her SSS score was reduced from 43.8 to 6.3 at 12 months. She did not have any treatment-related adverse events following the procedure.

Follow-up MRIs at 6 months were obtained in 30 patients with 33 fibroids. One patient underwent ultrasound instead of MRI. The rest of the 6 patients did not undergo the 6 months MRI due to following reasons: 1 patient underwent surgery, 2 are foreigners of which only 1 had MRI follow-up a year after treatment, 3 were lost to follow-up (did not turn up after treatment or after 6 months). The median fibroid volume of these 33 fibroids at 6 months after MRgFUS was 52 cm³ (95% CI, 39.5 to 78.4 cm³), which was significantly decreased by $41.6 \pm 23.2\%$ ($P < 0.001$) compared with those before treatment using Wilcoxon signed-ranks test (Fig. 4). However, in one patient, whose fibroid show 52.3% non-perfusion after treatment, there was an increase of 36.9% in volume at 6 months post-treatment. A second session of MRgFUS was performed at 7 months after the first session, and the fibroid volume still did not change 12 months later. This may be due to the very large fibroid volume (516.9 cm³) and the type of fibroid (intermediate type).

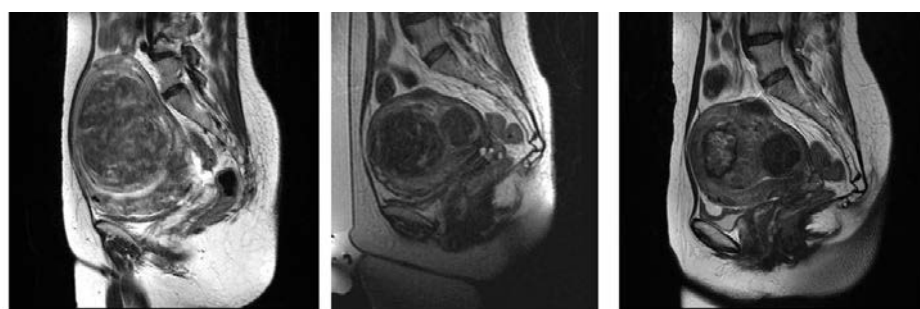
Follow-up MRI at 12 months was obtained in 12 patients with 15 fibroids. Eleven patients underwent ultrasound instead of MRI. Two patients underwent surgery, 1 patient became pregnant, 4 were lost to follow-up (did not turn up after 12 months). The median fibroid volume of these 15 fibroids at 12 months after MRgFUS was 34.4 cm³ (15.6 to 85.7 cm³, 95% CI), a significant reduction in volume by $52.6 \pm 26.1\%$ ($P < 0.005$, using Wilcoxon signed-ranks test) (Fig. 4).

The UFS-QOL Symptom Severity Scores

The SSS score was able to discriminate between normal participants and women with fibroids.¹² Women with fibroids experienced significantly higher levels of symptom distress and lower health-related quality of life than normal controls. The average SSS for normal women is 22.5, whereas patients with fibroids had an average score of 44.0. In our study, the mean SSS for the 37 patients was 41.7 ± 2.8 before treatment, indicating significant uterine fibroid related symptoms. In the overall study population, 13 evaluable patients had a 10-point or greater symptom improvement at 3 months after treatment, 19 patients had a 10-point or greater reduction of SSS at 6 months after treatment. The symptom improvement was maintained throughout 2 years and 3 to 4 years in 6 patients. As shown in Figure 5, the average SSS was 26.9 ± 3.6 , 20.7 ± 3.4 , 18.5 ± 3.6 , 16.5 ± 7.1 , 9.8 ± 3.6 at 3 months, 6 months, 1 year, 2 years and 3 to 4 years respectively. The decrease in scores was significant at all time points up to 3 to 4 years ($P < 0.05$ and $P < 0.001$). The use of auto-regressive model for repeated measurement indicated the significance of treatment effect.

Type of Fibroids

Based on the T2-weighted image signal intensities, the fibroids were classified into 3 types: dark, intermediate and white. We compared fibroid volume changes among the different types of fibroids before and after treatment. The intermediate type of fibroids had the largest median volume (164.1 cm³, 95% CI, 104.6 to 231.6 cm³) before treatment, whereas the median volumes of dark and white type of fibroids were 59.4 cm³ (95% CI, 42.9 to 106.1 cm³) and 82.3 cm³ (95% CI, 36.3 to 140 cm³) respectively (Fig. 6). At 6 months after MRgFUS, the size of dark and intermediate types of fibroids significantly decreased ($42.9 \pm 20.1\%$) and ($43.4 \pm 21.2\%$) respectively (Fig. 6). At 12 months after treatment, the dark and intermediate



(A) Pre-treatment T2-weighted image of the uterine fibroid. (B) Sagittal T2-weighted image of uterus on treatment day. (C) Six months post-treatment T2-weighted image showing sustained reduction of fibroid size

Fig. 3. Sagittal view of T2-weighted contrast-enhanced MRI from a 48-year-old patient over time. The images (A, B and C) show a time-dependent decrease in size of the intramural fibroid.

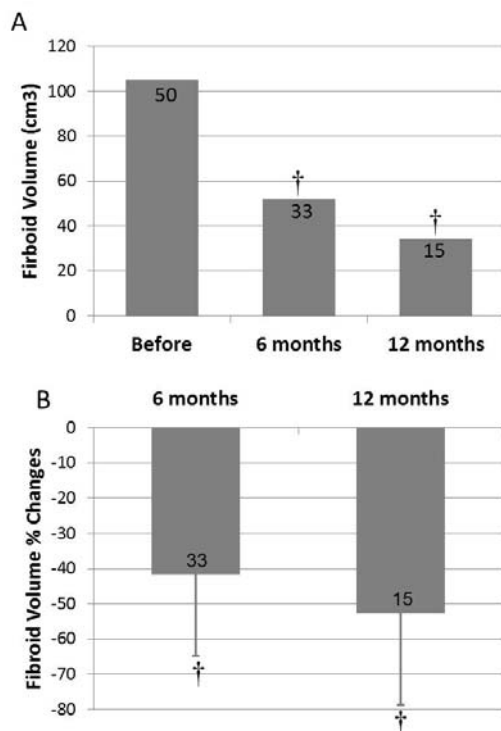


Fig. 4. Comparison of fibroid volume medians before and after treatment at 6 months and 12 months. (A) The fibroid volume medians comparison. Numbers inside the bars indicate number of fibroids. There was significant difference in fibroids volume between before and after treatments 6 months and 12 months. Bars in figure represent median volumes, $\dagger P < 0.001$. (B) The percentage changes of fibroid volume. Numbers inside the bars indicate number of fibroids. There was significant difference in percentage changes of fibroid volume before and after treatment 6 months and 12 months. Bars in figure represent mean percentage change in volume $\pm$ SD, $\dagger P < 0.001$.

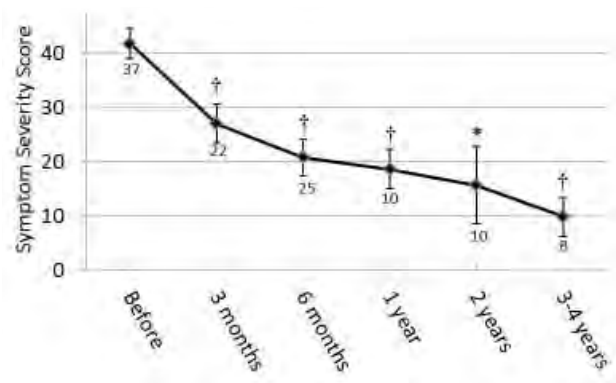


Fig. 5. Pair-wise comparison of UFS-QOL Symptom Severity Score (SSS) before and after treatment of 3, 6, 12 and 24 months. The numbers below the error bar are the number of patients. Auto-regression model for repeated measurement was used to measure the significance of treatment effect. $\dagger P < 0.001$, $* P < 0.05$.

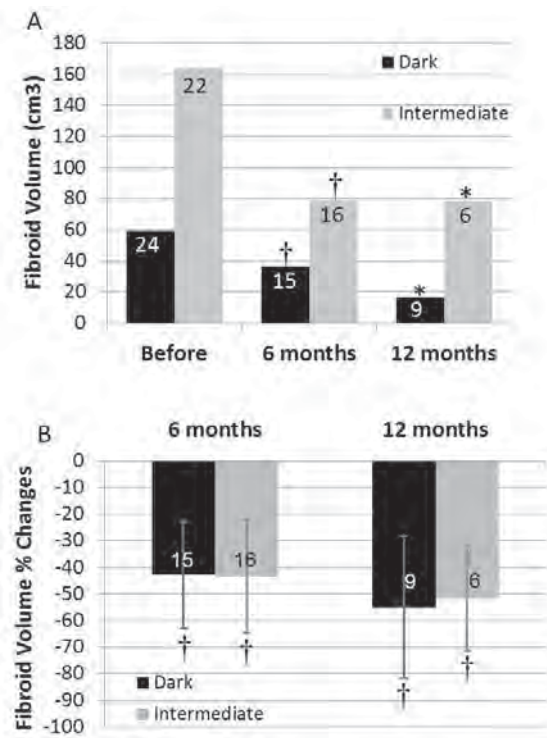


Fig. 6. Comparison of fibroid volume among different types of fibroids before and after treatment. (A) The fibroid volume medians comparison. Numbers inside the bars indicate number of fibroids. There was significant difference in fibroids volume between before and after treatments 6 months and 12 months. Bars in the figure represent median, $\dagger P < 0.001$. (B) Volume changes percentage of different types of fibroids. Numbers inside the bars indicate number of fibroids. There was significant difference of fibroids volume changes between before (as 100%) and after treatments 6 months and 12 months. Bars in the figure represent mean $\pm$ SD, $* P < 0.05$, $\dagger P < 0.001$.

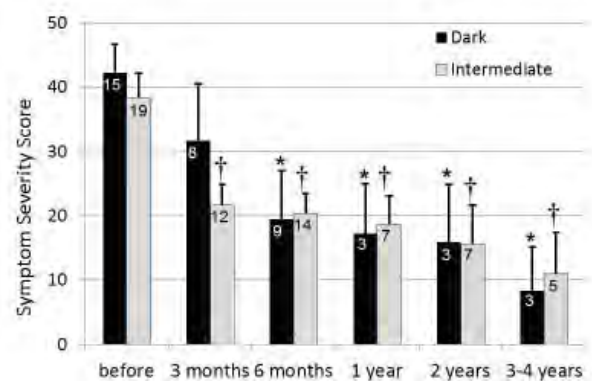


Fig. 7. Pair-wise comparison of Symptom Severity Score (SSS) changes of different types of fibroids before and after treatment. Numbers inside the bars are number of patients. Auto-regression model for repeated measurement was used to measure the significance of treatment effect. $\dagger P < 0.001$, $* P < 0.05$.

fibroids demonstrated significant reduction in size by ($55.1 \pm 26.7\%$) and ($51.8 \pm 19.8\%$) respectively (Fig. 6). There was no patient with white type fibroids evaluated at 12 months in this study.

We also compared SSS score changes among different types of fibroids before and after MRgFUS. Interestingly, the patients with white type of fibroids showed highest SSS score (60.4 ± 4.5) before treatment, indicating they suffer the most severe clinical symptoms, such as dysmenorrhoea, heavy menstruation, and pressure symptoms. There was no significant difference between the SSS scores of patients with dark and intermediate type fibroids (42.3 ± 4.3 , 38.3 ± 3.9 , respectively, Fig. 7). Correlation analysis between the type of fibroid and NPV, type of fibroid and SSS score reduction showed that 3-month SSS reduction was correlated with types of fibroid, $r = 0.414$, $P = 0.031$. In addition, 3-month SSS reduction was also correlated with NPV ratio, $r = 0.569$, $P = 0.071$.

Adverse Events

All patients, except 1, went home after 2 to 3 hours of observation. The only patient who was hospitalised after treatment had requested for it, although she was fit for discharge. Nurses made phone calls to patients daily during the first 2 to 3 days after MRgFUS. There was 1 serious adverse event of bowel perforation and nerve injury, requiring re-admission to hospital a day after the treatment, and subsequent surgery to the bowel. She eventually recovered. Analysis showed operator error and there was no equipment failure. The patient had a large fibroid that changed in configuration and position during the treatment, but this was not immediately recognised, resulting in error in targeting of the sonication. The patient also breathed in too deeply during each sonication, which resulted in the change in uterine fundal position. The lesson learnt from this incident is that the uterine outline and the sonication beam path must be carefully checked during each image acquisition in the course of the treatment. In the presence of significant changes in the target organ, the region of treatment must be revised by acquiring new MRIs. Minor complications included first degree burns on the abdomen in 2 patients and 1 patient who had mild foot discomfort recovered fully after 3 months. Other minor complaints included mild lower abdominal pain or discomfort related to either position within the magnet or uterine discomfort due to sonications. Apart from the patient with bowel injury, the rest of the patients returned to their normal activities within a few days after the procedure.

Discussion

MRgFUS has been approved for treatment of uterine

fibroids by the United States Food and Drug Administration (USFDA) in 2004. KKH was among one of the first worldwide to install the ExAblate 2000® system and currently is the only treatment centre in Singapore to perform this procedure. Since the first treatment in our centre in June 2006, almost all of the patients who have undergone this procedure were treated and discharged on the same day. With increasing numbers of patients seeking treatment options that allow them the least amount of disruption to their daily routine, the demand of minimally invasive or non-invasive treatment is clear and growing. Many studies have demonstrated that MRgFUS provided an effective, non-invasive and safe treatment option for uterine fibroids.^{9-11,15,16} However, there is a lack of long-term (up to 4 years) follow-up data after MRgFUS treatment. Based on a PubMed search on 30 July 2013, we are the second to report on long-term observation up to 3 to 4 years. Kim et al¹⁷ first reported the 3-year outcomes and showed sustained symptomatic relief among enrolled patients and there was no long-term complication.

In our present study, 76% (19 out of 25) of evaluated patients had a 10-point or greater improvement in their clinical symptoms at 6 months after treatment. The symptom improvement was maintained in 7 patients throughout 1 and 2 years, and in 6 patients over 3 to 4 years' duration. Our results are comparable with previous reports by Fennessy et al¹⁰ who demonstrated 10-points reduction in 74% of included patients at 6 months and in 73% of patients at 12 months. Using modified protocol that utilised larger ablation volume, the authors showed 10-points reduction in 88% of included patients at 6 months and in 91% patients at 12 months.

These clinical changes as well as the significant changes in the fibroid volume were observed although we included in this study all MRgFUS treatments performed. It should be borne in mind that these results were summarised from the first series of women who underwent this new treatment and the treated volume (NPV) was relatively smaller due to safety considerations. The later treatment with larger treated volume of fibroid tissues showed higher levels of improvement as some results indicated that the reduction in size might depend on the ablated volume.^{18,19} Steward et al²⁰ even developed a model indicating that probability of additional leiomyoma treatment was correlated with non-perfusion volume ratio. Fennessy et al¹⁰ compared the symptom relief between 2 protocols in which the averaged treatment fibroid volume ratio in original protocol was 16.7% whereas that in modified protocol was 25.8%. Better symptom relief was found in patients with modified protocol. Zhang et al¹⁹ showed there was no major adverse effect with the average treated fibroid volume ratio up to 75%. In our present study, the average treated fibroid volume (NPV) ratio was 54% and the 3-month SSS reduction was greatly correlated with NPV ($r = 0.569$, $P = 0.071$).

MRgFUS treatment led to a significant, time-dependent decrease in not only SSS, but also the mean fibroid volume. The average reductions in volume were 41.6% and 52.6% at 6 months and 12 months respectively ($P < 0.05$) which is comparable with other reports. Funaki et al²¹ demonstrated that mean decrease in fibroid size was 36.5% at 6 month and 39.5% at 24 month.

Most of the studies on MRgFUS conduct follow-up of the patients' symptoms at a regular time interval, i.e. 3 months, 6 month, 1 year, 2 years and so on. However, there is a lack of consensus on the appropriate time of follow-up for assessment of fibroid by MRI. Several reasons may contribute to this: (i) the cost of MRI is partly or fully borne by patients in Singapore, whereas it may be covered in other countries with more comprehensive medical insurance, (ii) although symptom improvement occurs as early as 3 months, it may not be consistent with the reduction of fibroid volumes. Further research needs to be done to address the optimal time point for evaluation of effectiveness of MRgFUS treatment.

An interesting finding in our study was that different types of fibroids were associated with different levels of severity of clinical symptoms. We classified the types of fibroids based on T2-weighted contrast-enhanced MRI. The highest pre-treatment SSS score was found in 4 patients with white type of fibroid whereas the lowest was found in the intermediate type. There was no significant difference between dark and intermediate type fibroids before treatment. Interestingly, the intermediate type of fibroid is the most responsive group in terms of volume reduction compared to other studies although this type of fibroids had the highest pre-treatment fibroid volume. Correlation analysis between the type of fibroid and NPV, type of fibroid and symptom severity reduction showed that 3-month SSS reduction was correlated with types of fibroid ($r = 0.414$, $P = 0.031$). Our results indicate that the classification of type of fibroid would help us to optimise the treatment protocol and predict treatment outcomes.

Recent findings from Zhao et al¹⁴ are in agreement with our results. The authors speculate that the white type of fibroids is predominantly cellular, while the intermediate type and dark type of fibroids that may contain tissue degeneration are less cellular and more fibrous.^{13,22}

In our study, 10 out of 37 (27%) patients underwent surgery at 2 years follow-up. All of them still had heavy and irregular menstruation at 6 months after MRgFUS treatment. Out of these 10 patients, 8 patients had large intermediate type of fibroids ($>200 \text{ cm}^3$), one patient had small white type of fibroid (56 cm^3) and one patient had small dark type of fibroid (70 cm^3) in the posterior wall. Out of 37 patients in our study, 3 patients underwent second

MRgFUS treatments. One patient had very large fibroid (517 cm^3) and after 6 months of first treatment, her fibroid enlarged to 700 cm^3 . After 6 months of second MRgFUS treatment, the volume her fibroid remained unchanged. She eventually went for hysterectomy after 2.5 years. Another patient had a hyperintense fibroid that also increased in size, and was found to have an endometrial stromal sarcoma. The third patient had an intermediate fibroid, but had sustained symptom improvement at 2 years.

Since the first clinical trial of MRgFUS treatment for uterine fibroids in 2003,¹⁵ the selection criteria have been broadened. For patients with bowel obstruction, simple measures such as rectal and bladder filling can effectively clear bowel away from the sonication beam path allowing for increased treatment ability. Recent development on the new generation of ExAblate® 2100 system has seen the implementation of several technical modifications and improvements. The transducer can be elevated close to the abdominal wall allowing for reduced energy density in the near and far field. Together with better energy dispersion, the maximum sonication spot size has been enlarged to 70 mm to facilitate treatment of larger fibroid volumes. Pre-treatment of large fibroids with a GnRH analog helps to reduce fibroid volume and increase fibroid tissue susceptibility to the treatment, which may improve MRgFUS outcomes.

Our study has several limitations. First, our patient population was relatively small. In addition, only a small number of patients returned their completed SSS questionnaires at 12 months and later. Evaluation of significance in treatment response over the longer durations is thus limited to the small group of patients. The questionnaires are valuable in assessing treatment response, and continue to be used routinely for all patients undergoing treatment, including those on long-term follow-up. Second, it was a single treatment arm trial. However, with emerging evidence on the outcomes of MRgFUS treatment, the selection criteria have evolved to make this procedure more broadly available to women who may benefit from it. Meanwhile, the treatment protocol has been optimised and redefined over the time. More patients will definitely benefit from this non-invasive, safe and effective treatment. Recent data on fertility after MRgFUS are promising and MRgFUS has potential to become the preconception treatment for uterine fibroids in asymptomatic women desiring to preserve their fertility.

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Aorto-oesophageal Fistula from Miliary Tuberculosis: A Rare Cause of Massive Haematemesis

Dear Editor,

Aorto-oesophageal fistula (AEF) is a rare surgical emergency that is often lethal. Primary causes described include thoracic aortic aneurysm¹ and carcinoma of the oesophagus.² Secondary causes include foreign body ingestion³ such as chicken and fish bones, surgical instrumentation, and procedures such as oesophageal biopsy,⁴ and erosion from aortic bypass grafts.⁵ In this case report, we describe a patient with AEF who presented with massive haematemesis from an oesophageal lesion found on endoscopy.

Case Report

A 46-year-old Filipino female presented to the emergency department in shock after 2 episodes of haematemesis at home. She did not have a history of foreign body ingestion. Investigations showed anaemia with a haemoglobin level of 6.4 mg/dL, but electrolytes and liver function tests were otherwise normal. A chest x-ray done was initially thought to be normal, but later was reported as having bilateral interstitial markings suggestive of possible infective change (Fig. 1).

She was brought to the endoscopy centre for emergency oesophagogastroduodenoscopy (EGD), which demonstrated large amounts of fresh blood and clots in the stomach. The oesophagus was not visualised well. During the procedure, the patient had cardiovascular collapse and developed pulseless electrical activity. She was therefore transferred

to the operating theatre for emergency surgery. At this point, it was assumed that the source of the bleeding was from the stomach or duodenum secondary to peptic ulcer disease.

At laparotomy, a gastrostomy was performed and bleeding was found to be coming from above the cardio-oesophageal junction. An on-table EGD was performed, and an actively spurting vessel was seen at 25 cm from the incisors. Attempts were made at endoscopic haemostasis with haemoclips and adrenaline injection without success. Insertion of a Sengstaken–Blakemore tube for tamponade also failed to arrest the bleeding. An intraoperative angiogram was performed on-table to identify the bleeding vessel, with a view to angio-embolisation. Unfortunately, due to poor cardiac output, the fistula was not well visualised except for a small area of abnormal vasculature near the area of haemorrhage. The impression then was a vascular malformation causing massive haemorrhage.

The patient had multiple episodes of cardiovascular collapse intraoperatively despite massive blood product transfusions and this led to her eventual demise.

At the postmortem examination, she was found to have disseminated miliary tuberculosis involving multiple organs including the kidneys and the lungs. The cause of AEF was found to be a necrotic nodule interposed between the aorta and oesophagus measuring about 3 cm in diameter. Several other small lymph nodes with miliary tuberculosis were seen in the region of the nodule. The pleural surfaces of both lungs were also heavily studded with miliary nodules.

Discussion

AEF are relatively rare, but almost universally fatal. There are few reported cases of survival. The patient usually has a history of recent foreign body ingestion or recent interventional procedures such as an oesophageal biopsy. The most common causes are thoracic aneurysms (51%), foreign body ingestion (19%), and oesophageal carcinoma.⁶

Tuberculous disease of the gastrointestinal (GI) tract can present in different ways. Other than bleeding, it may also present as intestinal obstruction.⁷ There are multiple published reports of tuberculosis-associated GI bleeding. Depending on the aetiology and location of the pathology, the patient may present with upper or lower GI bleeding.

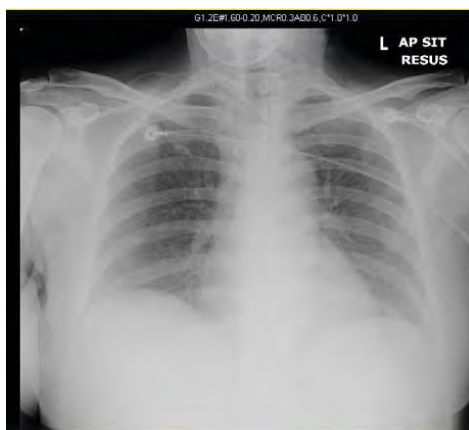


Fig. 1. Chest x-ray performed at admission.

Tuberculosis may affect the organs of the GI tract directly;⁸ it may also result in pseudoaneurysms or mycotic aneurysms of adjacent vessels with subsequent involvement of the GI tract, such as a jejunal artery pseudoaneurysm involving the jejunum;⁹ tuberculous mediastinitis can erode into the oesophagus and aorta, causing haemorrhage into the oesophagus presenting as upper GI bleeding. In the case described here, tuberculous mediastinitis resulted in erosion into both the oesophagus and aorta with formation of an AEF.

Tuberculous AEF is uncommon. Fistulae secondary to tuberculous esophagitis have been reported,¹⁰ but only 1 case secondary to tuberculous mediastinitis has been described in literature by Lee et al.¹¹ In that case report, the patient survived the initial surgery having undergone an Ivor–Lewis procedure, but succumbed to pulmonary complications about 2 months postoperatively.

Here, we describe a case of primary AEF as a complication of mediastinal tuberculosis. The patient had miliary tuberculosis that was not diagnosed at initial presentation. She presented with massive upper bleeding GI tract and haemorrhagic shock. The nodule of mycobacterium infection presumably eroded through the aorta and the oesophagus, resulting in a fistula and massive haemorrhage.

The management for AEF has been previously described.^{12,13} Different methods have been used, including aortic graft replacement and esophagectomy with both primary and delayed oesophago-gastro anastomosis.¹⁴ For fistulae secondary to thoracic aneurysms, aortic stent grafting for initial haemostasis, followed by open surgical aortic segment replacement and interval oesophageal repair have been described.¹⁵

Successful management requires a high index of suspicion with prompt diagnosis and arrest of bleeding with subsequent stabilisation of the patient. Although rare, the diagnosis of AEF should be considered in a patient presenting with massive upper GI bleeding. Tuberculous disease should also be considered in patients from areas where tuberculosis is endemic.

The chest x-ray findings of possible infective changes were subtle and missed initially. The diagnosis of tuberculosis was thus only made at postmortem. The implication of making this diagnosis only at postmortem was that several healthcare workers were potentially exposed to miliary TB and had to consider post-exposure prophylaxis.

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Transient Ischaemic Attack as First Presentation of Polycythaemia Vera

Dear Editor,

Cerebrovascular disease (CVD) consists of an age-dependent spectrum of transient ischaemic attack (TIA), cerebral infarction and haemorrhage. It is the second leading cause of death globally, and fourth in Singapore, accounting for 10% to 12% of all deaths.¹ TIA is defined by the American Heart Association and American Stroke Association as a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischaemia, without acute infarction.² We reported an interesting but rare case of TIA secondary to polycythaemia vera (PV). We also reviewed the literature and discuss management guidelines of PV in the emergency department (ED).

Case Report

A 65-year-old Chinese male, ex-smoker and hypertensive, presented to the ED after a transient episode of right-sided limb numbness and weakness, facial droop, dizziness and dysphasia. His symptoms resolved spontaneously within 15 minutes.

He was hypertensive with blood pressure of 177/91 mmHg. Physical examination and electrocardiogram were unremarkable. His ABCD2 score was 3. Initial investigations revealed a normochromic, normocytic erythrocytosis with haemoglobin (Hb) of 20.4 g/dL, red blood cell count of $6.56 \times 10^{12}/L$ and haematocrit (Hct) of 61.6%. His white cell, platelet counts, renal and liver function tests were normal. Magnetic resonance imaging (MRI) of the brain showed no acute infarct or intracranial haemorrhage. He was admitted to our observation ward and reviewed by a haematologist who diagnosed PV based on the World Health Organization (WHO) criteria (Hb >18.5 g/dL and/or Hct >60%). His erythropoietin level was normal. The diagnosis of PV was further corroborated by the *Janus Kinase 2 (JAK 2)* mutation test which proved him to be a heterozygous mutant. This test affirmed our diagnosis according to the Polycythemia Vera Study Group (PVSG) criteria. He was started on aspirin 100 mg once daily, simvastatin 20 mg once at night and hydroxyurea 500 mg twice daily. He underwent 2 consecutive venesections and currently attends regular outpatient haematological follow-up.

Discussion

ED patients with a history suggestive of TIA undergo a standardised protocol of investigations, which include basic laboratory studies, electrocardiogram and brain imaging.³ The main management aims for ED patients with suspected TIA are stratification of stroke risk, identification of treatable causes or conditions that can mimic symptoms of TIA. Laboratory testing is essential to exclude any reversible metabolic abnormalities and haematological disorders e.g. thrombocytosis.

PV is a rare but treatable cause of cerebral ischaemia in the Asian context. Thus far, only 1 Asian case had been reported.⁴ PV is suspected as a potential source of cerebral ischaemia in TIA patients aged 45 or below with a history of clotting dysfunction, multiple venous and arterial occlusions, suspected or confirmed cancer, or family history of thrombotic events.² The diagnosis of our patient, however, is made more challenging. There were no symptoms or signs, and no family history to suggest or increase the suspicion of PV. Hence, all emergency physicians (EPs) should maintain a high level of suspicion for the rarer causes of CVD including PV, especially when there is erythrocytosis or an elevated Hct level. EPs play a vital role in diagnosing and initiate early treatment in PV. Urgent therapeutic and preventative treatment including venesection should be commenced to prevent the development of organ infarction.

Patients with TIA in the ED are risk stratified for stroke development using the ABCD2 scoring system. Low risk patients receive aspirin and an urgent outpatient neurological referral. The National Stroke Association recommends admission for those with conditions which predispose them to a higher risk of stroke like atrial fibrillation, hypercoagulable state, crescendo TIAs, and high risk of early stroke after TIA stratified using the ABCD2 i.e. score 6 to 7.2. Our patient's ABCD2 score of 3 did not satisfy the admission criteria but he was admitted because of the suspicion of PV; a hypercoagulable state. This again emphasised the importance of careful interpretation of the Hb and Hct levels in our patient who would otherwise be discharged from the ED.

PV is a chronic myeloproliferative disorder with an annual incidence of 2.3/10,000 cases. The mean age of presentation

is around 60 years with a slight male predominance. It is associated with panmyelosis.⁵⁻¹⁰

The 2 main diagnostic criteria for PV are the WHO and the PVSG criteria; the latter are listed in Table 1. However, in patients with *JAK2* mutation, like our index case, a diagnosis of PV becomes valid in the presence of high Hct (>50% in men and >48% in women) or an increased red cell mass of >25% above the predicted value.⁸ In *JAK2* gene mutants, production of blood cells is multiplied and their survival is prolonged. Approximately 96% of PV patients have *V617F* mutation.^{11,12} Peripheral blood screening for *JAK2* mutation is now the first-line test for evaluation of suspected PV. Concomitant measurement of serum erythropoietin levels (which is known to be decreased in more than 90% of newly diagnosed PV) is also recommended.¹³

Erythrocytosis leads to a hyperviscous state; predisposing patients with PV to an increased risk of thromboembolic events with an annual risk of thrombosis at 3%. The risk of thromboembolism rises in a linear relationship with the Hct level and stroke/TIA, myocardial infarction, deep venous thrombosis/pulmonary embolism are the most common thromboembolic events. Management of PV is based on risk stratification of developing thrombotic events⁸ as detailed in Table 2.

Cerebral blood flow is significantly reduced in PV patients. Venesection reduces blood viscosity by lowering the venous Hct to <45%; at which cerebral perfusion improves by 73%.^{6,7} Low dose aspirin is also recommended unless contraindicated. Other treatment options such as cytoreduction have shown benefits in the management of patients with thrombocytosis. Hydroxyurea has shown effectiveness in myelosuppression as well as risk reduction of thrombosis compared to venesection alone for patients above the age of 40.^{6-10,13}

Table 1. Polycythaemia Vera Study Group Criteria

A1: Raised red cell mass; male >36 mL/kg, female >32 mL/kg
A2: Normal arterial oxygen saturation >92%
A3: Splenomegaly
B1: Platelet count >400 x 10 ⁹ /L
B2: White blood cell count >12 x 10 ⁹ /L
B3: Leucocyte alkaline phosphatase >100
B4: Serum B12 >900 pg/mL or unbound B12 binding capacity >220 pg/mL
Diagnosis
A1 + A2 + A3 establishes PV
A1 + A2 + 2 of category B establishes PV

In *JAK2* mutants, the diagnosis of PV becomes valid with a high haematocrit (>50% in men and >48% in women) or an increased red cell mass of >25% above the predicted value.

PV: Polycythaemia vera

Table 2. Risk Stratification and Treatment Algorithm of Polycythaemia Vera According to Thrombotic Risk

Risk	Risk Factors	Treatment
High	Age ≥60 or previous thrombosis	Venesection + low dose aspirin + cytoreductive treatment (hydroxyurea)
Intermediate	Age <60 and no previous thrombosis, but with a. Thrombocytosis (<1500 x 10 ⁹ /L) b. Cardiovascular risk factors • Cigarette smoking • Diabetes • Hypercholesterolaemia c. Hypertension	Venesection + low dose aspirin
Low	None of the above	Venesection + low dose aspirin

Conclusion

EPs need to be aware of PV as a rare but treatable cause of TIA with an excellent outcome. The clinical clues to PV may be minimal and careful interpretation of the Hb and Hct levels is decisive.

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