TAN TOCK SENG HOSPITAL

MEDICAL DIGEST

OCTOBER - DECEMBER 2017

Tan Tock Seng
HOSPITAL

11 Jalan Tan Tock Seng
Singapore 308433

Tel: 6256 6011
Fax: 6252 7282

www.ttsh.com.sg

Medical Digest is a quarterly publication of Tan Tock Seng Hospital written by healthcare providers for healthcare providers, as a service to the medical community.

Tan Tock Seng
HOSPITAL

MCI (P) 094/08/2016

FROM THE EDITOR

A generation ago, in 1987, two hundred eager, naïve young doctors were unleashed in the five government hospitals extant in Singapore. I was one of them! I only know it now, but it is peculiar to Singapore then that almost all the doctors in all the public hospitals hail from the same school. As everything in life, we started at the bottom, did the grunge work, endured the scolding and secretly vowed to become better than our seniors.

The most fun time to practice Medicine in hospitals is probably just after having passed the postgraduate examination and being a new registrar. We were energetic and confident of our skills. The best thing was that, after hours, the entire hospital, if not every medical institution in the country, was run by a classmate. Need an urgent scan? Need rare blood-type transfusion? Need someone to go in to stop a bleeder? No problem.

In these three decades, we saw many changes in government policies, medical understanding, and medical practice. Heck, we made some of them ourselves so they cannot be all bad!

Like whisky produced by different distilleries, though everything began as fermented barley water, the final product is the same but different. We all had different trajectories in life and career. Some remain in public service, most are in private practice. Most are working humbly (like yours truly) and a few have achieved prominence. A handful of classmates have made countries other than Singapore their homes. Four classmates have fallen to illness.

To the NUS Medicine class of 87, it's been a great privilege to have spent five years with you. I love you all, including those with whom I have never spoken to. If I could go back in time …

Dr Leong Khai Pang
EDITOR
Medical Digest

MEDICAL DIGEST

EDITOR
Leong Khai Pang

ASSOCIATE EDITORS:
Charmaine Manauis
Raymond Ng
Melissa Tien
Mohd Fadil Muhammad Farhan

MEMBERS:
Tang Yee Lin
Rafael Saclolo
Ivan Huang Kuang Hsin
Noorhazlina bte Ali
Deshan Kumar
Tan Choon Chieh
Shirley Bang
Chong Yaw Khian
Kalaiyarasi Kaliyaperumal
Adeline Teh
Yew Min Sen
Shirlene Ho Shu Min
Gavin Lim Hock Tai
Binedell Trevor Brian

COPY EDITOR
Safiyya Mohamed Ali

DESIGNER
Clinton Low

We value your feedback. Please email your questions, comments or suggestions to:
ttsh_ccs@ttsh.com.sg
Please also contact us for notification of change of postal address or requests of additional copies.

TTSH RESEARCH NEWS

Every year, TTSH clinicians publish about 300 scientific papers. In this section, we selected a few reports and asked one of the authors of each to summarise and discuss the clinical relevance of their research. The theme this issue is the surgical disciplines.

IMPORTANCE IN CLINICAL PRACTICE

IOP is one of the most important known modifiable factors in the management of patients with glaucoma. Earlier studies have reported decrease in IOP following cataract extraction in both normal and glaucomatous eyes but these studies reported only the change in IOP of the surgical eyes and not the fellow eyes. There is therefore a question of whether the reported decrease in IOP may be confounded by diurnal fluctuations of IOP or regression to the mean. One strength of our study is the measurement of IOP in both eyes over 2 years. This allows us to observe the long-term changes in IOP of the fellow eye both prior to and after cataract extraction. Having the fellow eye as control minimises the confounding effect of diurnal variation and regression to the mean. In addition, we are one of the few to report this effect in an Asian population. In summary, we described a 2-year sustained and statistically significant mean decrease in IOP of approximately 2.0 mmHg after cataract surgery which represents more than 10% decrease compared to baseline values. We therefore believe that cataract extraction may be beneficial in a multi-faceted approach to IOP control in selected individuals.

RESEARCH EXCERPT 1

Effect of bilateral sequential cataract extraction on intraocular pressure in non-glaucomatous Asian eyes

Ngo WK, Tan CS. Br J Ophthalmol. 2016; 100(4):560-4.

We conducted a review of 116 non-glaucomatous patients with sequential bilateral cataract extractions. We found sustained and statistically significant ($p<0.001$) decrease in intraocular pressure (IOP) in the surgically treated eye compared to fellow (control, non-operated) eye for up to 2 years. Mean decrease in IOP ranged from 1.6 (8.6%) to 2.3 mmHg (14.0%). In contrast, the IOP in the fellow eye remained unchanged. Subsequently, when surgery was performed in fellow eye, the IOP decreased by a similar amount, and was similarly sustained. The decrease in IOP is of greater magnitude in eyes with higher pre-surgical IOP and is not affected by the type of surgery, whether phacoemulsification or extracapsular cataract extraction. The effect of IOP decrease after surgery is unilateral and does not affect the fellow eye.

This summary was prepared by Dr Ngo Wei Kiong, a consultant in the Department of Ophthalmology, Tan Tock Seng Hospital.

RESEARCH EXCERPT 2

Cardiopulmonary resuscitation – from the patient's perspective

Wee S, Chang ZY, Lau YH, Wong Y, Ong C. Anaesth Intensive Care. 2017; 45(3):344-350.

Locally, end-of-life discussions prior to hospitalisation are uncommon, in part due to conservative Asian cultures and values. When patients deteriorate, they are often physically or mentally incapable of communicating their treatment preferences. Hence, the duty of making end-of-life decisions regarding resuscitation falls into the hands of physicians or the patient's immediate family, using the principles of substituted judgement or the patient's best interest.

Existing literature reveals that surrogate decision-makers have poor knowledge of basic resuscitation options, and the surrogates' decisions often differ markedly from the patients' own preferences.

Though there is scant literature on this topic in Singapore, two recent papers confirmed the incongruence of surrogate's versus patient's decisions, and that discussions of end-of-life issues with patients were infrequent.

We used an 18-item questionnaire to study patients' knowledge, attitudes and preferences regarding cardiopulmonary resuscitation (CPR). We administered this questionnaire to patients with no or minor medical conditions, more than 24 hours after elective surgery in the day surgery ward of Tan Tock Seng Hospital, in April and May 2015. The median age was 58 years and more than half had post-secondary education. This was a relatively well and clinically stable cohort of patients, which we think is representative of the community-dwelling population.

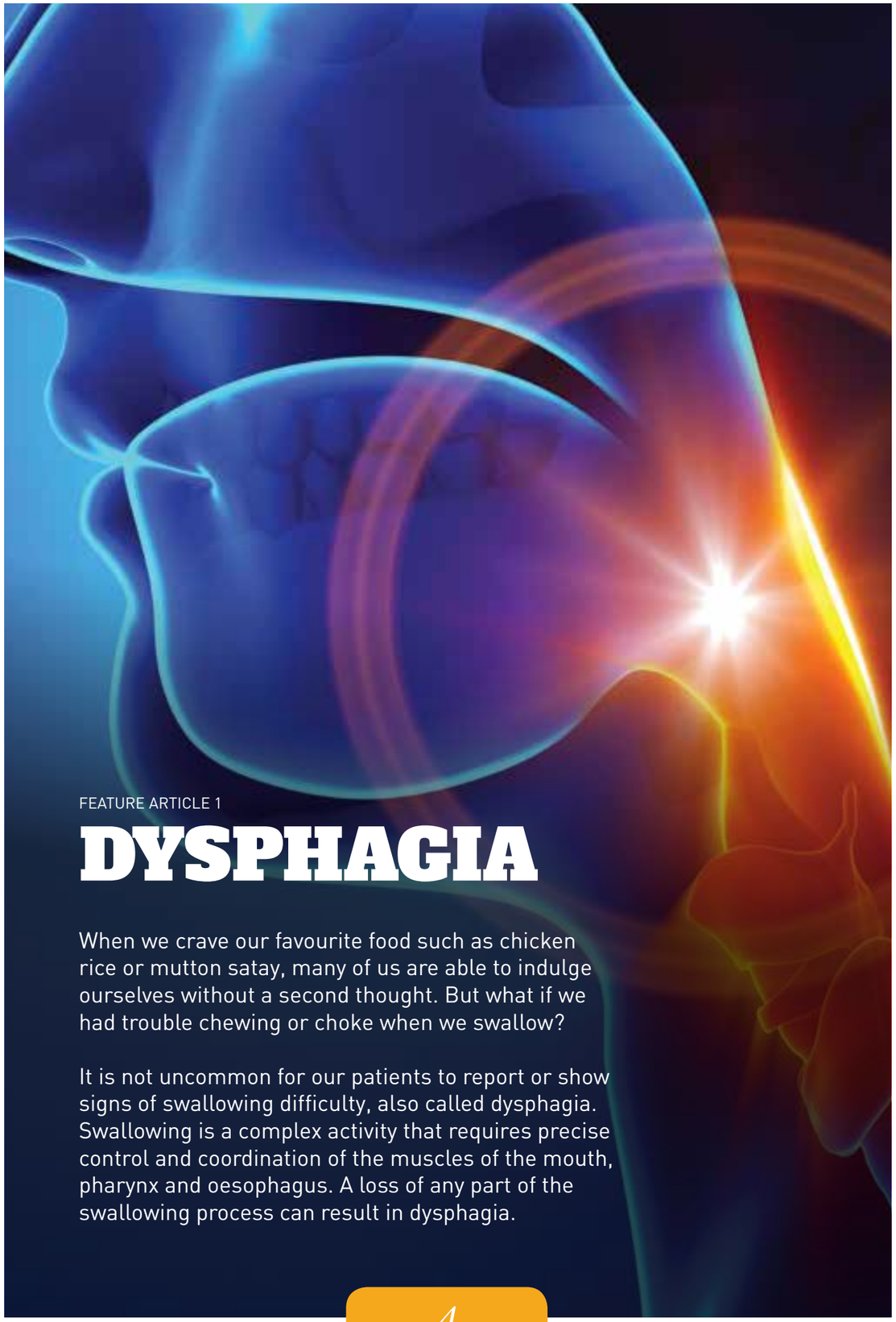
We found that participants had poor understanding of the process of CPR, its components and potential complications, and they grossly overestimated the success rate of CPR. Forty-one percent of the participants had previously given thought to the life support measures they would want for themselves but 75% had never discussed this with anyone. 86% felt that they should personally be involved in their end-of-life decisions. 84% had a desire to receive more information on this topic.

This summary was prepared by Dr Caroline Ong Yu Ming, a consultant in the Department of Anaesthesiology, Intensive Care & Pain Medicine, Tan Tock Seng Hospital.

IMPORTANCE IN CLINICAL PRACTICE

Care planning is an important but commonly neglected part of holistic care. Timely communication regarding end-of-life issues appears to be inadequate, and most patients had poor knowledge of CPR and other resuscitative measures. However, the majority were keen to improve their knowledge and to discuss end-of-life issues with physicians.

The shared end-of-life decision making process can be improved so as to accurately reflect patients' true wishes. Physicians must facilitate a frank, accurate and realistic discussion with patients and families to improve their understanding of resuscitation options and their success rates. By doing so, the ethical and emotional burdens faced by both physicians and relatives as surrogate decision-makers at the point of a medical crisis may be reduced, and the subscription rates for advance medical directives may improve. The patient's autonomy is thus maintained up to the final moments.



FEATURE ARTICLE 1

DYSPHAGIA

When we crave our favourite food such as chicken rice or mutton satay, many of us are able to indulge ourselves without a second thought. But what if we had trouble chewing or choke when we swallow?

It is not uncommon for our patients to report or show signs of swallowing difficulty, also called dysphagia. Swallowing is a complex activity that requires precise control and coordination of the muscles of the mouth, pharynx and oesophagus. A loss of any part of the swallowing process can result in dysphagia.

Who can get dysphagia?

Dysphagia is common in the elderly particularly those with dementia. Individuals at risk of dysphagia are those with stroke, head injury, neurological conditions (such as Parkinson's disease and motor neuron disease), head and neck cancer, respiratory illnesses (such as chronic obstructive pulmonary disease) and functional decline.

Signs and symptoms of dysphagia

These are the features of dysphagia:

- Difficulty in chewing food;
- Frequent throat clearing, coughing or choking during or after swallowing;
- Wet or gurgled voice quality during or after meals;
- Sensation of food stuck in the throat;
- Shortness of breath during or after meals;
- Excessive drooling or food lost from the mouth;
- Nasal regurgitation (food or fluid flows up into the nose);
- Swallowing multiple times for each spoonful;
- Increase in phlegm production during or after meals;
- Taking a long time to finish a meal;
- Refusal to swallow;
- Food left in the mouth after swallowing;
- Recurrent episodes of right-sided pneumonia;
- Unexplained weight loss; and
- Chest discomfort when swallowing.

Consequences of dysphagia

Aspiration pneumonia is a constant concern for individuals with dysphagia. Aspiration occurs when food or fluid (including saliva) enters the airway and lungs. Aspiration pneumonia can be fatal.

Individuals with dysphagia can become malnourished and dehydrated. Choking may result in phobia of drinking and eating. Loss of appetite may result from the intake of modified food and drinks, leading to inadequate intake.

Swallowing assessments

If you suspect that your patient has dysphagia, you should promptly refer him or her to a speech therapist, a professional qualified to assess and treat this condition. In hospitals, doctors and trained nurses perform the water swallow test as a screen before referring patients to the speech therapy services. This test assesses the safety and readiness of the patient for oral feeding and determines whether further swallowing assessment is required. This test can be done in the community if general practitioners or nurses have undergone training.

The speech therapist will carry out a detailed assessment to identify the nature and extent of the patient's swallowing problems. The assessment enables the speech therapist to identify the best method of feeding (oral versus non-oral), the consistency of food and drinks that the individual should swallow to minimise the risk of aspiration, appropriate feeding strategies and potential swallowing rehabilitation.

Clinical assessment of swallowing is often supplemented with imaging studies (endoscopy and/or fluoroscopy). The management plan is then developed according to these clinical and instrumental findings.

If you suspect that your patient has dysphagia, you should promptly refer him or her to a speech therapist, a professional qualified to assess and treat this condition.

Videofluoroscopy

Videofluoroscopy is an instrumental procedure using X-rays to evaluate dysphagia. It is used to assess swallowing ability, determine the safest food and fluid consistencies that can be consumed and identify effective swallowing strategies. The procedure is usually performed by a speech therapist in conjunction with a radiologist or radiographer. The individual is seated for the procedure and given small

Type of solid food diet	Description	Example
i) Easy chew diet	Food that is soft, tender and moist, usually chopped to about 1.5 cm x 1.5 cm in size and cooked longer to soften it. Chewing is required.	Firm tofu, steamed fish, soft rice 
ii) Soft moist diet	Food that is soft and finely minced and that it can be easily mashed using the tongue. Minimal chewing is required.	Oats, porridge, minced meat, silken tofu 
iii) Blended diet	Food that is smooth and lump-free. A blender is needed for food preparation. No chewing is required.	Mashed potato, blended porridge, sesame paste 

Table 1. Table of modified consistencies for solid foods.

Type of fluid	Description	Gum-based thickeners	Starch- based thickeners
i) Nectar thick	Fluid pours quickly off a spoon but slower than normal drinks. Effort is required to drink through a standard bore straw. Examples: Thick barley drink, mango juice		
ii) Honey thick	Fluid flows easily from spoon when tilted and does not stick to the spoon. Effort is required to suck through a wide bore straw. Example: honey		
iii) Pudding thick	Fluid able to hold shape on spoon and must plop off when spoon is tilted. Cannot be drunk from a cup and cannot be sucked through a straw. Example: thick plain yoghurt		

Table 2. Table of modified consistencies for fluids.

amounts of barium coated food and fluid of different consistencies to swallow. The entire procedure typically takes about 15-20 minutes.

Fibreoptic Endoscopic Evaluation of Swallowing

Fibreoptic endoscopic evaluation of swallowing is an instrumental procedure in which a flexible endoscope is inserted through the nose to observe the airway at the level of the larynx during swallowing. Small amounts of food and fluids of different consistencies

are stained with food dye to allow better visibility. The entire procedure lasts approximately 20-30 minutes.

Management of dysphagia

The speech therapist may recommend modified food textures and fluid consistencies. For instance, a softer diet texture may be recommended if the individual has difficulty chewing hard food while thickening liquids helps to control the speed, direction, duration and clearance of the liquids facilitating safe swallowing for individuals with reduced tongue movement and slow swallows. Examples of modified solid foods (table 1) and thickened fluid consistencies (table 2) are depicted below. Thickeners available in the market are largely gum-based or starch-based. Gum-based thickeners are commonly used in the acute hospital setting as they are more stable and do not thin down when in contact with enzymes in saliva which break down components of starch.

Non-oral feeding

Non-oral feeding may be recommended when an individual has severe swallowing difficulties and is at high risk of developing aspiration pneumonia. Non-oral feeding can also be considered if oral intake is insufficient to meet nutritional and hydration needs. Malnutrition contributes to several health problems, including heart and blood vessel disease, deterioration of mental status and the immune system, and poorly healing pressure ulcers and wounds.

The two most common forms of non-oral feeding are feeding via a nasogastric tube and percutaneous endoscopic gastrostomy. The formula feeds and feeding schedule for these methods of feeding are commonly prescribed by the dietician or the doctor.

While non-oral feeding methods provide direct benefit in many clinical situations, they do not benefit all patients with dysphagia or inadequate nutritional intake. There is growing evidence that tube feeding for patients with advanced dementia does not prevent aspiration pneumonia, prolong survival, reduce the risk of pressure sores or infections, improve function, or provide palliation. Furthermore, the presence of alternate feeding methods can cause a cascade of negative psychosocial features, including depression and loss of social interaction associated with feeding. In addition, it can also result in increased use of physical restraints to prevent patients from removing enteral feeding tubes. Hence, the practice of tube feeding in the end stages of degenerative illnesses in the elderly should be carefully considered. The eventual decision on the mode of feeding is made in conjunction with the individual, his caregiver(s) and the medical team.

Rehabilitation for dysphagia

Therapy exercises are recommended to help maintain the individual's swallowing ability, improve swallowing physiology and to delay the progression of the swallowing disorder. The individual with dysphagia and his/her carer (if applicable) will be taught various tasks that can improve the individual's swallowing ability. These therapy tasks need to be carried out repeatedly by the individual on a regular basis as suggested by the speech therapist to yield positive therapeutic outcomes.

The frequency of reviews and therapy with the speech therapist is dependent on the needs of the individual. These reviews help to ensure that the individual is eating and drinking safely, and that swallowing therapy is on track and progress is being made, making adjustments where necessary.

Compensatory strategies

Speech therapists may recommend intervention strategies, termed "compensatory strategies", which are intended for short-term use in the individual who is anticipated to improve. These strategies help the individual cope with dysphagia in the short term, while keeping in view the long-term goal of maintaining nutrition and hydration.

Oral care

Individuals with dysphagia and poor oral health are at higher risk of aspiration pneumonia. They often have reduced ability to manage their own secretions and require more attention to maintain oral hygiene. Poor oral hygiene may result in an increased amount of oral bacteria that may be aspirated during swallowing or at rest. Regular oral and dental care helps to minimise bacteria in the mouth, and in turn, minimise the impact of aspiration. Products such as antiseptic mouth wash, oral swabs, non-foaming toothpastes and other alcohol-free products may be included in daily oral care. Xerostomia (dry mouth) can occur in individuals with dysphagia and cause discomfort. The use of oral moisturisers can provide relief.

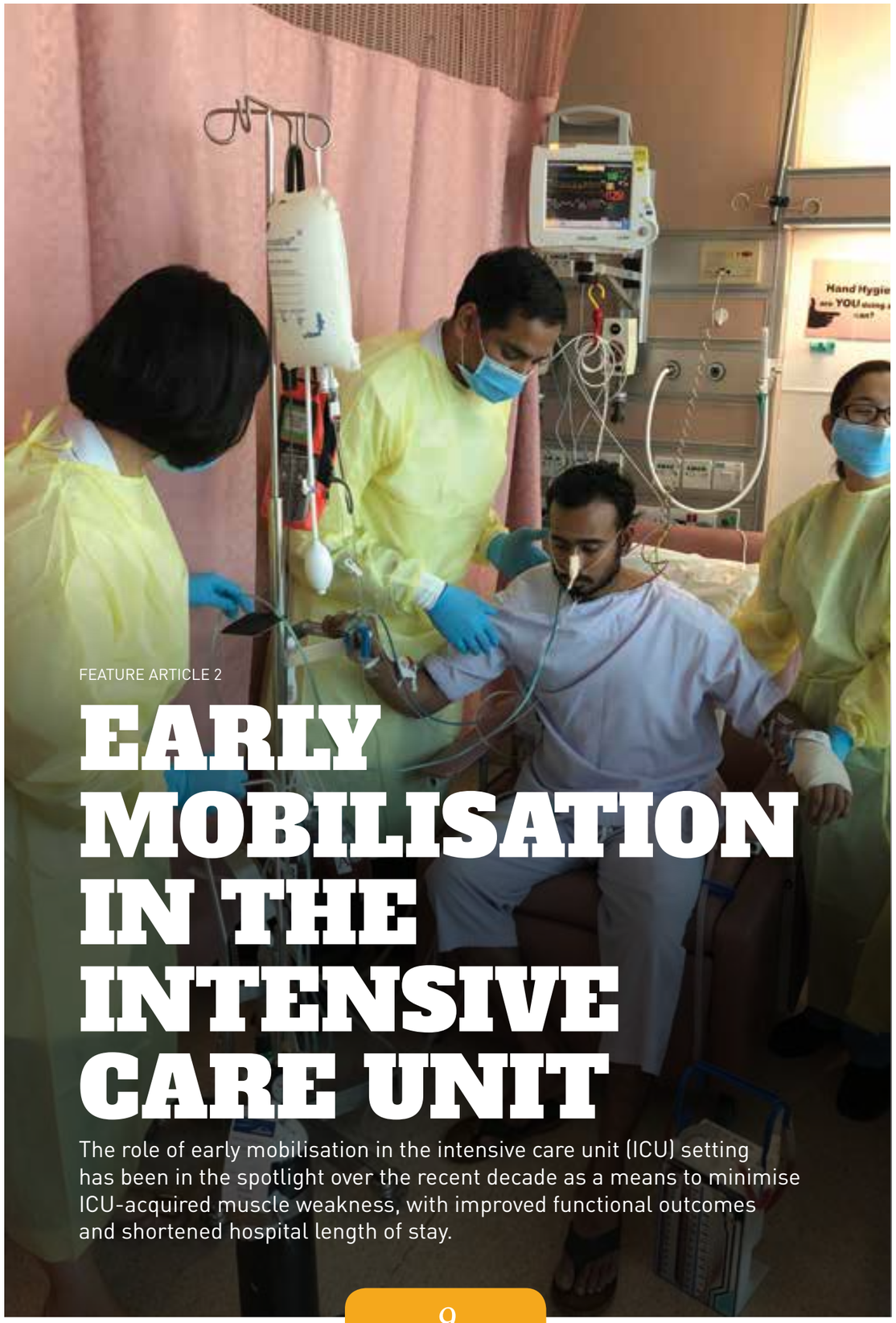
The management of dysphagia requires the coordinated expertise of a number of health care professionals, including the primary care physician, speech therapist, dietician, occupational therapist, physiotherapist, nurse, dentist, as well as the primary caregiver. The goals are to optimise the safety, efficiency and effectiveness of the swallow, to maintain adequate nutrition and hydration, as well as to ensure good oral hygiene. Wherever possible, the enhancement of quality of life should be taken into account during management.

While non-oral feeding methods provide direct benefit in many clinical situations, they do not benefit all patients with dysphagia or inadequate nutritional intake. There is growing evidence that tube feeding for patients with advanced dementia does not prevent aspiration pneumonia, prolong survival, reduce the risk of pressure sores or infections, improve function, or provide palliation.

FURTHER READING

1. *Cichero JA, Murdoch BE, editors. Dysphagia: foundation, theory and practice. John Wiley & Sons; 2006.*
2. *Logemann JA. Dysphagia: evaluation and treatment. Folia Phoniatr Logop 1995; 47(3):140-64.*

MS KAREN CHIN CHIEN LING
is a speech therapist in the Department of Speech Therapy, Tan Tock Seng Hospital.



FEATURE ARTICLE 2

EARLY MOBILISATION IN THE INTENSIVE CARE UNIT

The role of early mobilisation in the intensive care unit (ICU) setting has been in the spotlight over the recent decade as a means to minimise ICU-acquired muscle weakness, with improved functional outcomes and shortened hospital length of stay.

Having understood the importance of early mobilisation, a multidisciplinary team led by Dr Jonathan Tan from Tan Tock Seng Hospital went to Johns Hopkins Hospital, Baltimore, to learn from experts in the field of early ICU mobilisation. Subsequently, the team started facilitating early mobilisation in the TTSH surgical ICU in a small group of patients. The team then proposed a quality improvement initiative to widen the reach of early mobilisation in an attempt to improve clinical care of patients in ICU. The quality improvement initiative brought a multidisciplinary team of doctors, nurses, physiotherapists and respiratory therapists together. The team worked together to come up with a checklist to identify suitable patients who are ready to start early mobilisation, and implemented a protocolised early mobilisation care plan (table 1). The checklist broadly covers three areas: establishing the patient's medical stability (including stable blood pressure and heart rate); predicting the patient's ability to participate in the therapy session (including the level of alertness and ability to obey simple commands); and assessing whether the patient has adequate muscle strength in the arms and legs to sit and stand.

The checklist was disseminated to the ground staff and training was provided through hands-on actual patient screening. With continuous practice the nurses were able to screen the patients on their own without the help of the physiotherapist. The nurses were also keen to learn how to mobilise the patients on their own so that they could do it even when

1. Premorbid - independent ambulation
2. ICU stay ≥ 3 days
3. CNS (RASS +1 to –1; Muscle power ≥ 4/5)
4. CVS (no vasopressors; no new arrhythmia or cardiac ischaemia in the past 12 hours)
5. Respiratory system: Ventilated PEEP< 8; $FiO_2 \leq 50\%$ Non-ventilated $FiO_2 \leq 50\%$; RR≤ 24
6. No surgical contraindications
7. Pain score ≤ 5/10

Table 1. Checklist to determine suitable patients who are ready to start early mobilisation.

the physiotherapist was not around. Thus, training sessions were conducted for the nurses and this enabled them to independently mobilise the patient to sit in a chair (figure 1). This was a big culture change and it led to patients being mobilised in a timely manner and enabled the physiotherapist to spend more time on standing and walking activities with the patient (figure 2).

There were some hiccups along the way which led to a fall in the number of mobilisation exercises. One of the reasons was inadequate communication between staff. For example, the therapist may not know that a central venous pressure line was recently

Figure 1. Patient prepared to mobilise out of bed post-operatively.

Figure 2. Patient being assisted to ambulate.

removed and the patient needs to rest in bed, or that the patient was transferred to a different ward or to the operating theatre. A communication board was introduced to allocate dedicated time for mobilisation and allow for smooth planning. This helped to get the rates of mobilisation back on target. There was also a mandatory weekly mobilisation ward round with all stakeholders to discuss cases suitable for mobilisation. As a result of these concerted efforts, surgical intensive care mobilisation was sustained at 100 percent for all eligible patients. The team has found that patients who were started on early mobilisation were discharged from the ICU earlier, with their average length of stay in the ICU reduced by two days. Also, these patients went on to demonstrate higher rehabilitation potential upon discharge and regained function quickly at a community setup.

After the safe and successful implementation of the programme in the surgical ICU, early mobilisation has now been implemented in the medical ICU, as well as the high dependency care unit. We are now a founding member of the Asia-Pacific Early Mobilisation Network, where we hope to play our part in spreading this care programme.

This early mobilisation initiative by TTSH was selected to contest in the Asian Hospital Management Awards in 2014. It received the Gold Award under the Clinical Improvement category for its role in service improvement and improved patient outcomes. Additionally, this project was publicised in local newspapers such as The Straits Times, *Tamil Murasu*, and *Berita Harian*. This was indeed a morale-boosting recognition for the entire team and surgical ICU staff. This initiative has since been sustainable and has achieved much success towards the early recovery of patients.

The team has found that patients who were started on early mobilisation were discharged from the ICU earlier, with their average length of stay in the ICU reduced by two days. Also, these patients went on to demonstrate higher rehabilitation potential upon discharge and regained function quickly at a community setup.

One such example is Mr Liao, a 61-year-old Chinese gentleman who was admitted to the TTSH ICU following a motorcycle accident that left him with arm fractures, as well as spine and spleen injuries. He spent 40 days in the ICU and needed the support of a ventilator. With the early mobilisation programme, he was able to get out of bed to sit up in a chair while in the ICU. As his strength gradually returned, he was able to walk assisted even when he was on ventilator support. Even with the fluctuations in his medical condition, which is very much expected in an ICU environment, he was able to walk with the help of a walking aid when he was being transferred to a normal ward after his long ICU stay. This may not have been possible without the early mobilisation programme. In an interview with the Chinese local newspaper *Zaobao*, Mr Liao said, "I was very worried about my mobility after the accident but after receiving early physiotherapy in the ICU, it has enabled me to move! I feel better and am slowly regaining my muscle strength and coordination to go back to walking and doing the things I love!".

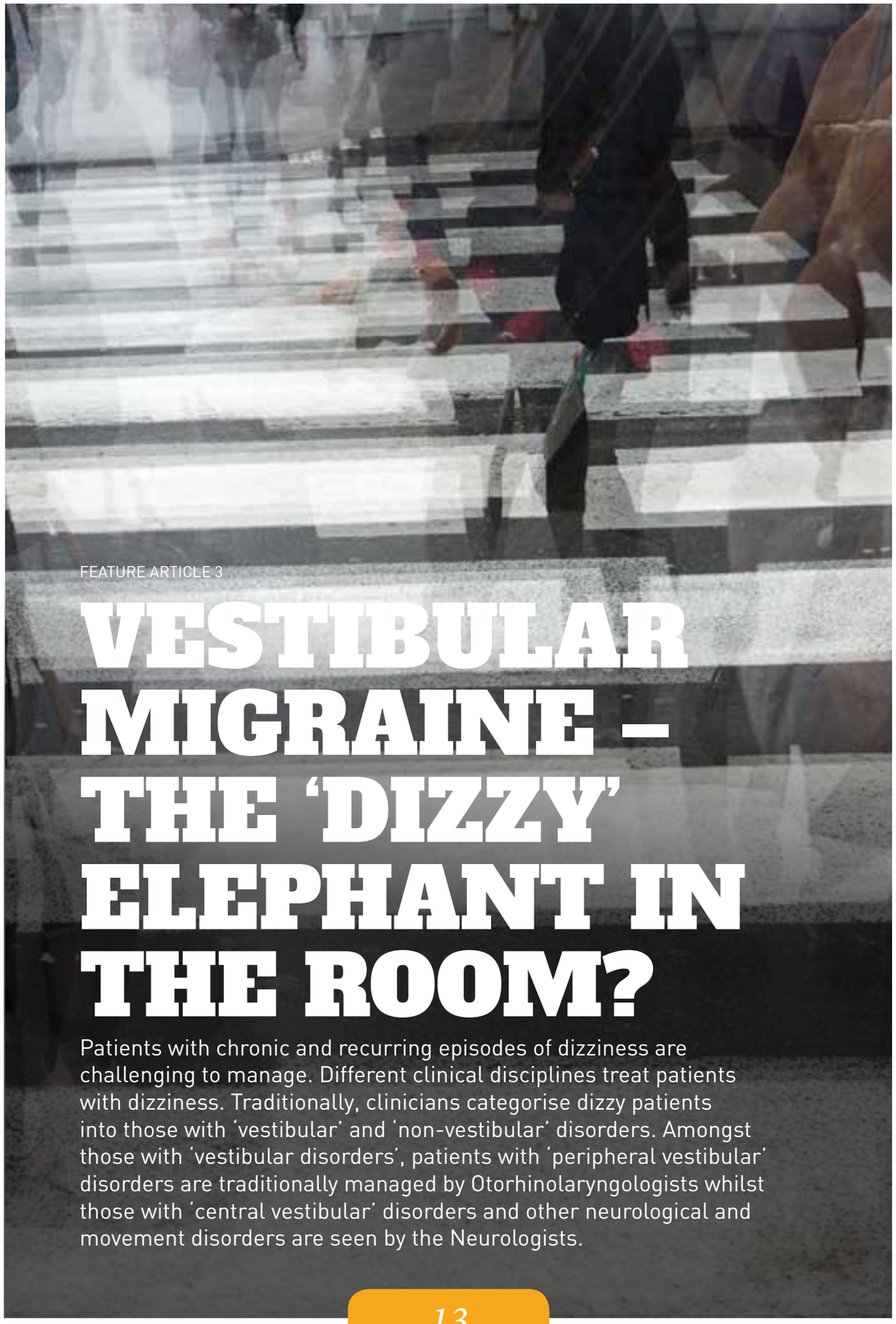
There are some challenges in attempting early mobilisation. For example, there will be days when the patient has to rest in bed due to medical reasons. When this happens, the mobilisation exercises will have to be re-started. Overall however, early mobilisation has been shown to confer expressed benefits towards patients within the ICU setting. With the effective implementation of these protocols with strong interdisciplinary teamwork, we can expect to see enhanced critical care and improved patient outcomes.

"I was very worried about my mobility after the accident but after receiving early physiotherapy in the ICU, it has enabled me to move! I feel better and am slowly regaining my muscle strength and coordination to go back to walking and doing the things I love!".

FURTHER READING

1. *Adler J, Malone D. Early mobilization in the intensive care unit: a systematic review. Cardiopulmonary physical therapy journal. 2012;23(1):5-13.*
2. *Bailey P, Thomsen GE, Spuhler VJ, Blair R, Jewkes J, Bezdjian L, et al. Early activity is feasible and safe in respiratory failure patients. Crit Care Med. 2007;35(1):139-45.*
3. *Hanekom S, Gosselink R, Dean E, van Aswegen H, Roos R, Ambrosino N, et al. The development of a clinical management algorithm for early physical activity and mobilization of critically ill patients: synthesis of evidence and expert opinion and its translation into practice. Clinical rehabilitation. 2011;25(9):771-87.*
4. *Morris PE, Goad A, Thompson C, Taylor K, Harry B, Passmore L, et al. Early intensive care unit mobility therapy in the treatment of acute respiratory failure. Crit Care Med. 2008;36(8):2238-43.*
5. *Needham DM. Mobilizing patients in the intensive care unit: improving neuromuscular weakness and physical function. Jama. 2008;300(14):1685-90.*
6. *Needham DM, Korupolu R, Zanni JM, Pradhan P, Colantuoni E, Palmer JB, et al. Early physical medicine and rehabilitation for patients with acute respiratory failure: a quality improvement project. Archives of physical medicine and rehabilitation. 2010;91(4):536-42.*
7. *Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. Lancet (London, England). 2009;373(9678):1874-82.*
8. *Thomsen GE, Snow GL, Rodriguez L, Hopkins RO. Patients with respiratory failure increase ambulation after transfer to an intensive care unit where early activity is a priority. Crit Care Med. 2008;36(4):1119-24.*

MR JAYACHANDRAN BALACHANDRAN
is a principal physiotherapist in the Department of Physiotherapy, Tan Tock Seng Hospital.



FEATURE ARTICLE 3

VESTIBULAR MIGRAINE – THE 'DIZZY' ELEPHANT IN THE ROOM?

Patients with chronic and recurring episodes of dizziness are challenging to manage. Different clinical disciplines treat patients with dizziness. Traditionally, clinicians categorise dizzy patients into those with 'vestibular' and 'non-vestibular' disorders. Amongst those with 'vestibular disorders', patients with 'peripheral vestibular' disorders are traditionally managed by Otorhinolaryngologists whilst those with 'central vestibular' disorders and other neurological and movement disorders are seen by the Neurologists.

For the 'non-vestibular' group of patients, physicians from various specialties like Internal Medicine, Cardiology and Geriatric Medicine are involved if the underlying diagnosis is syncope or pre-syncope (iatrogenic, vaso-vagal, cardiac arrhythmias, etc.) or general frailty from multiple medical problems. This list is far from exhaustive. For example, the Endocrinologist may be involved if there are diabetic patients with peripheral or autonomic neuropathy or the Ophthalmologist for patients with visual impairment.

Role of our balance system

Our balance system is vital to our orientation and survival within earth's environment that has a gravitational field. It allows us to maintain an upright posture and facilitates bipedal gait. Our balance system also stabilises our visual perception for us to interact with our environment, allowing us to feel steady despite the repetitive and fast natural movements of our head or movements in our surroundings. Our balance system, like our breathing and heart contraction, works automatically and is taken for granted until it malfunctions.

Anatomy and physiology of balance

To understand balance disorders, it is useful to remind ourselves of the normal anatomy and physiology of our balance system. There are three components in our balance system; the afferent component, the central nervous system (CNS) and the efferent component. Our balance **afferent component** has three main sensory inputs: vestibular, from the three semi-circular canals and the two otolithic organs located within each vestibule of our inner ear; visual from our eyes; and somatosensory from our proprioceptive and sensory receptors within our lower limbs, neck and other joints. The **CNS component** including the brain stem and cerebellum helps integrate and modulate the balance sensory inputs. Two vital reflexes work with the efferent balance components to complete the system. The vestibular-ocular-reflex has the six extra-ocular muscles as its **efferent component** and this important reflex helps us maintain visual stability. The vestibular-spinal-reflex has the anti-gravity and peripheral muscles as its **efferent component** and is vital for us to maintain postural and gait stability.

For both reflexes, the vestibule provides the afferent signals and hence any dysfunction with this organ

The pattern of the vertigo will help distinguish the different conditions. For BPPV, the vertigo is positionally induced, has a latency, lasts less than a minute, is fatigueable and is recurrent as long as the disease is active.

gives rise to specific dizziness symptoms. At rest, in a normal person, there is no net difference between both vestibules and hence, there should be no involuntary eye movement. Any acute loss (common) or over-activity (less common) of one vestibule can lead to a unilateral afferent vestibular hypofunction or hyperfunction that results in the acute asymmetry of the vestibular-ocular-reflex. This results in the 'temporary' involuntary repetitive movement or deviation in the patients' eyes, clinically observed as 'jerky nystagmus' (clinical sign elicited by clinicians) and perceived as vertigo; defined as the 'perception or hallucination of movement where there is none' (symptom as described by patients). Vertigo as per its strict definition has been the cardinal symptom in the management of peripheral vestibular disorders by Otorhinolaryngologists.

Jerky nystagmus has a slow and fast phase and with the direction of the fast phase conventionally defined as the direction for the nystagmus. The clinical finding of a jerky nystagmus is a hallmark of an acute peripheral vestibular asymmetry and follows Alexander's laws. The direction of the nystagmus should be away from the hypofunctioning side and the intensity of the nystagmus should also be

accentuated (with no change in nystagmus direction) when gaze is directed away from the hypofunctioning side. And, the intensity of the nystagmus should be increased when visual fixation is removed with the use of very high dioptic glasses. In contrast, central type nystagmus tends to be pendular (i.e. no fast and slow phase) and direction-changing depending on gaze direction. Patients with central type nystagmus frequently do not experience concurrent vertigo.

Peripheral vestibular disorders

The 'big' three diagnoses for the Otorhinolaryngologists are benign paroxysmal positional vertigo (BPPV), Meniere's disease, and acute vestibular hypofunction (from vestibular neuronitis, labyrinthitis or a thromboembolic event within the inner ear). In all three conditions, patients report vertigo as a symptom and jerky nystagmus should be elicited during clinical examination, when patients are symptomatic. Hearing loss and tinnitus will be present if the cochlear is involved (e.g. labyrinthitis) and for Meniere's disease, the presence of aural fullness will complete the clinical picture.

The pattern of the vertigo will help distinguish the different conditions. For BPPV, the vertigo is positionally induced, has a latency, lasts less than a minute, is fatigueable and is recurrent as long as the disease is active. For Meniere's disease, the vertigo usually lasts minutes to several hours, but can be recurrent during the active phase. Patients with either of these two conditions can get recurrent vertigo episodes but they tend to be fairly asymptomatic in between the active periods.

However, for acute vestibular hypofunction, the vertigo is usually non-recurrent. The vertigo is often severe, with associated nausea and vomiting that lasts up to a day but rarely beyond. However, the patient can remain dizzy for days to weeks afterwards, pending central compensation for the asymmetrical vestibular input. They are rarely vertiginous beyond the first 24 hours, but suffer from dizziness in the form of imbalance and disequilibrium, head-motion-provoked dizziness and visual-provoked dizziness i.e. induced by excessive movements of their surroundings or being in a visually complex or stimulating environment (such as when watching action movies, or walking in a visually stimulating environment like a supermarket aisle or corridors and passages with repetitive patterns or lines).

Most of these symptoms often diminish once the patients centrally compensate for the acute vestibular hypofunction. For young patients, this tends to happen within days to weeks so long as they are not on a prolonged course of vestibular sedatives like prochlorperazine or cinnarizine that hamper the brain's natural balance compensatory mechanism. Older patients who are slow to compensate centrally and those who have developed an overdependence on their visual inputs for their balance will benefit from vestibular rehabilitation exercises. These are provided by specially trained physiotherapists who are able to provide 'substitution' and 'adaptation' type exercises to compensate for the 'lost' vestibular function and also 'habituation' type exercises for head motion and visual sensitivity.

There are rarer conditions that affect the inner ear, e.g. superior semi-circular canal dehiscence and auto-immune inner ear disease or AIED, that result in recurrent vertigo attacks in patients, but often with other otological symptoms. Patients with AIED usually have symptoms in both ears. It is unwise and unsafe to follow the outdated adage that *'it is not a vestibular problem if there is no vertigo'*. Patients with bilateral vestibular hypofunction do not experience vertigo if there is no asymmetry in their peripheral vestibular function. Instead, they are highly intolerant to any head movement and they actually perceive their entire surroundings bouncing up and down each time they try to walk. This is termed ossilopsia and can be highly disabling. One of the commonest causes of bilateral vestibular hypofunction is ototoxicity due to aminoglycoside antibiotics and platinum chemotherapy agents.

Additionally not all patients with unilateral vestibular hypofunction experience vertigo. As mentioned earlier, most patients with acute vestibular hypofunction experience dizziness symptoms rather

than vertigo beyond the first 24 hours. Another example is the patient with chronic progressive vestibular hypofunction. Patients with vestibular schwannoma will often experience slow, progressive loss of vestibular function unilaterally. The slow pace of vestibular decline allows progressive central compensation and hence most of these patients have neither vertigo nor imbalance.

The Multi-Disciplinary Balance Clinic at Tan Tock Seng Hospital

There is no substitution for a comprehensive history and examination to arrive at the correct diagnosis. The Tan Tock Seng Hospital Multi-Disciplinary Balance Clinic (MBC) was started in the first half of 2012 to manage patients with complex balance and dizziness symptoms. Patients in this clinic are seen concurrently by an Otorhinolaryngologist, Vestibular Therapist and Audiologist. The focus of this clinic is to offer an accurate diagnosis followed by a comprehensive, holistic, personalised and actionable treatment plan. There is also an ongoing engagement with cross-referrals to other clinical teams for example, the Neurologists, the Psychologists and the 'Falls Clinic' which is run by Geriatricians. Over time we will develop an 'Interdisciplinary Balance Network' to better manage patients with complex dizziness disorders.

The 'chronic vestibulopathy' patients

Within the Multi-Disciplinary Balance Clinic, it soon became clear that there is a large cohort of patients who do not fit nicely into any of the common or rarer peripheral vestibular dysfunction diagnoses. Many of these patients have had chronic recurrent dizziness episodes over many years or even decades. Some of these patients needed multiple in-patient admissions with each stay lasting longer than two nights. Many more had needed multiple trips to the Emergency Department or Family Physicians. These recurrent attacks of dizziness can severely impact the patients' quality of life. Many had to give up all forms of exercise and some have lost the confidence to leave the confines of their homes. A few patients have had to give up working or struggle in their primary role as a parent or caregiver. Some have developed secondary anxiety and depression from their unremitting symptoms.

Many of these patients had acquired diagnoses like 'chronic vestibulopathy', 'chronic vertigo', 'non-specific dizziness' and 'multi-factorial dizziness' prior to being seen in the MBC. These diagnoses are deeply unsatisfying and unhelpful to both physicians and patients. Whilst they are descriptive of the patients' symptoms, they do not provide any aetiological nor pathophysiological explanation into their problems. Some patients are put onto long-term vestibular sedatives like cinnarizine which often make things worse.

Many more are on long-term betahistine which is a histamine agonist with variable results. A large proportion of patients are also referred to the Vestibular Therapists. Whilst they may be able to improve patients' functional status without a firm clinical diagnosis, some symptoms like head-motion- and visual-provoked giddiness remain challenging to address. More importantly, without an accurate diagnosis, patients will not receive the relevant advice on the prevention and management of future episodes of dizziness. Many patients state that the unpredictability and the lack of understanding of their diagnosis or the lack of diagnosis, for that matter, can result in loss of confidence, anxiety and excessive worrying. This impacts their quality of life massively.

The elephant in the room

One should be alert to the possible diagnosis of vestibular migraine for patients where no firm balance diagnosis can be made especially after multiple encounters with various health care professionals. Vestibular migraine has maintained a rather enigmatic status despite the many published papers on this condition. Vestibular migraine is a diagnosis given to a subset of patients with migraine who suffer from dizziness which is aetiologically related to their migraine. The publication of a Consensus Diagnostic Criteria by the Barany Society and International Headache Society in 2012 has helped to provide clarity in the diagnosis and management of this condition. In fact, there has been a multitude of terminology used for this diagnosis previously including 'migraine-associated dizziness' or MAD and 'migrainous vertigo' or MV. One wonders if the choice of the former acronym reflects scepticism on the part of the clinicians.

Clinical history

Patients with vestibular migraine suffer from recurrent episodes of dizziness that last between 5 minutes to 72 hours. These episodes of dizziness include vertigo which may be spontaneous, brought on by head motion or head position changes, or induced by visual stimulus. Some patients with non-vertiginous dizziness induced by head motion are described as having 'disturbed spatial orientation'. These symptoms are usually severe enough to interfere with or stop daily activities. However, to make this diagnosis, patients also need to have either a current or previous history of migraine with or without aura. Also, at least half of the dizziness episodes should be associated with at least one of the following: migraine-pattern headaches, photophobia and phonophobia, or visual aura. Last but not least, other dizziness diagnoses must be excluded. A diagnosis of probable vestibular migraine can also be made if the spectrum of symptoms is less than complete.

From my personal experience, the commonest symptoms amongst patients with vestibular migraine are head-motion-provoked and visual-provoked dizziness which may or may not be vertiginous. A strong sense of nausea or vomiting are both common. These are often brought about by any activity that involves head movement including something as benign as running or rushing about. Patients are very reluctant to move their heads and avoid bright, crowded and noisy places during the attacks. Like traditional migraine patients, they will seek a dark, quiet place to rest during attacks. Most patients do not get concurrent headaches although they may get headaches or head heaviness in between the dizziness attacks. A smaller number of patients experience recurrent dizziness attacks without any in-between headaches.

However, for this group of patients who are usually older, a careful history will elicit a previous history of recurrent headaches, with or without dizziness. These headaches could have started as early as their primary school days but with resolution or reduction in their 40s and 50s. This is something for them to celebrate. Unfortunately, after a period of minimal symptoms, they start to suffer from recurring episodes of dizziness. Some patients do complain of head heaviness, which can be at the front, top of head, back of head and sometimes all over the head, rather than the classical unilateral throbbing pattern which they are likely to have suffered when younger.

Many patients also suffer from motion sickness, which can precede their headaches and dizziness for many years. They report difficulty in reading on the bus, going up spiral carpark ramps, or riding

roller coasters when young. There is frequently a strong family history of recurrent headaches and/or dizziness.

Another useful aspect of the history to explore is the relationship between migraine triggers and dizziness attacks. The commonest lifestyle triggers for vestibular migraine are tiredness and lack of sleep, stress, negative emotion like anxiety, worry or depression. Unfortunately, these lifestyle triggers are often inter-related and many patients enter a vicious cycle, culminating in clinical depression and anxiety. Dietary triggers like monosodium glutamate, salt, caffeine, chocolate and alcohol are frequently reported as well. Two other important triggers are dehydration and peri-menstrual periods.

Examination findings

Patients with vestibular migraine do not have spontaneous or gaze-evoked nystagmus. A complete examination includes checking the ears for any acute or chronic ear infective or inflammatory condition. Central examination includes checking for smooth pursuit and saccadic eye movements and cerebellar function. It is vital to exclude vestibular hypofunction as some of the clinical signs may actually overlap. For example, the Halmagyi Head Thrust can sometimes be positive as some patients find it extremely difficult to maintain their gaze. However, interestingly, some vestibular migraine patients are found to have this test positive bilaterally. The differential diagnosis then is bilateral vestibular hypofunction.

For the Dynamic Visual Acuity or DVA test, both vestibular migraine and vestibular hypofunction patients will have a drop of four lines or more. There are three tests that can help differentiate between these two conditions. Post-head-shake nystagmus tends to be positive only in patients with vestibular hypofunction, even in those who had it in the past and have centrally compensated. The Foam Romberg's test is also useful. Patients with vestibular migraine tend to be able to maintain their balance even with their eyes shut. Patients with vestibular hypofunction will almost always fall down, frequently to their hypofunctioning side. The last test is the Unterberger's test where patients with true vestibular hypofunction tend to deviate that side during the test.

Investigations

Vestibular migraine is a clinical diagnosis and the role for investigations is limited. In fact, there is no single investigation that will confirm its diagnosis. However, investigations can be useful to rule out other diagnoses like vestibular hypofunction or Meniere's disease. For most patients, an audiogram to confirm normal hearing is helpful. A Video Head Impulse Test (VHIT) can help exclude vestibular hypofunction, whilst an MRI scan of the cerebello-pontine angle can exclude a vestibular schwannoma.

Vestibular migraine is a clinical diagnosis and the role for investigations is limited. In fact, there is no single investigation that will confirm its diagnosis. However, investigations can be useful to rule out other diagnoses like vestibular hypofunction or Meniere's disease.

Management

It has been immensely useful and rewarding to explain the diagnosis, its aetiology and natural history to most patients. Many of them are desperate for a good explanation for their chronic symptoms. It is often necessary to spend time explaining the lifestyle and dietary trigger factors. But not all patients are able to change longstanding behavioural and dietary habits. And it is certainly not fair to tell the insomniac to just try and sleep more when they have difficulties falling asleep or suffer from early wakening. Pharmacotherapy options should always be explored, and from my experience, more than 90% of patients are willing to try medication, especially if you assure them that the aim is to avoid long term medication.

Using asthma medication as an analogy is very helpful to the patients. They need to understand the two main types of medication which are the prophylaxis and relieving or abortive. For the latter, many patients who continue to get headaches will respond to either paracetamol or NSAIDs. Second-line medication like the triptans and caffeine plus ergotamine tend to be effective as well. Interestingly, most patients who get concurrent dizziness with their headaches also report relief of their dizziness with these abortive medications. However, their role in relieving dizziness that does not occur with headaches is less clear.

For migraine prophylaxis, there are five or six different classes of medication. There is no clear-cut 'most effective medication' on reviewing the literature.

There is a high variability in different centres, let alone different countries, in clinicians' first and second choices. If one is uncomfortable with using anti-convulsants like topiramate or sodium valproate, there are alternatives. The main three medications that I use as migraine prophylaxis are propanolol (a beta-blocker), nortriptyline or amitriptyline (tricyclic anti-depressant) and flunarizine (calcium channel blocker). It is vital to understand the side effects and contra-indications for these medications.

The commonest medication I use for younger patients is propranolol, after excluding the main contra-indication of asthma, symptomatic hypotension and impaired cardiac function. For older patients, low-dose nortriptyline and amitriptyline are my first choices. Side effects include daytime somnolence and mouth dryness. Contra-indications include bladder outlet obstruction and constipation. Flunarazine tends to work for patients who do not tolerate the other two medications. Side effects include insomnia and weight gain.

A large proportion of vestibular migraine patients have chronic insomnia. It is useful to observe that most of them experience a significant improvement in their sleep pattern after starting low-dose nortriptyline or amitriptyline. This often coincides with a significant improvement in their dizziness and/or headache symptoms. However, many complain about the daytime somnolence. Taking the medication 12 hours before their intended wake-up time seems to lessen this side effect. The dosage that maximises the positive effect and minimises side effects is highly variable between patients. Patients are advised to titrate their dosage between 5 and 30 mg to find their ideal balance. Most patients are on 5 or 10 mg of either medication daily.

Patients are often encouraged to take their prophylactic medication for 2 to 3 months initially to confirm the efficacy of the medication. Resolution or improvement in dizziness symptoms helps to confirm the diagnosis. Most patients are reluctant to be on long-term medication and hence, they are advised to stop the prophylaxis after they have addressed their lifestyle and dietary migraine trigger factors.

Many patients go through periods where their lifestyle and/or dietary factors are not conducive, resulting in a flare-up of their migraine symptoms. Fortunately, these are usually easy to predict. For students, these would be around examinations and for working people, around deadlines and other work surges. Many of them are willing to take their migraine prophylaxis medications only during these stressful periods.

There is a small group of patients with significant anxiety and/or depression due to their chronic and unremitting dizziness symptoms. Besides all the treatment modalities, they are also offered a consultation with the Clinical Psychologist. Many of these patients will fail to achieve full control of their migraine symptoms if their psychological well-being is not addressed. Many of these patients fall into the spectrum of persistent-postural-perceptual-dizziness or PPPD disorder that was originally described by Jeffrey Stabbs, a Psychiatrist from the Mayo Clinic.

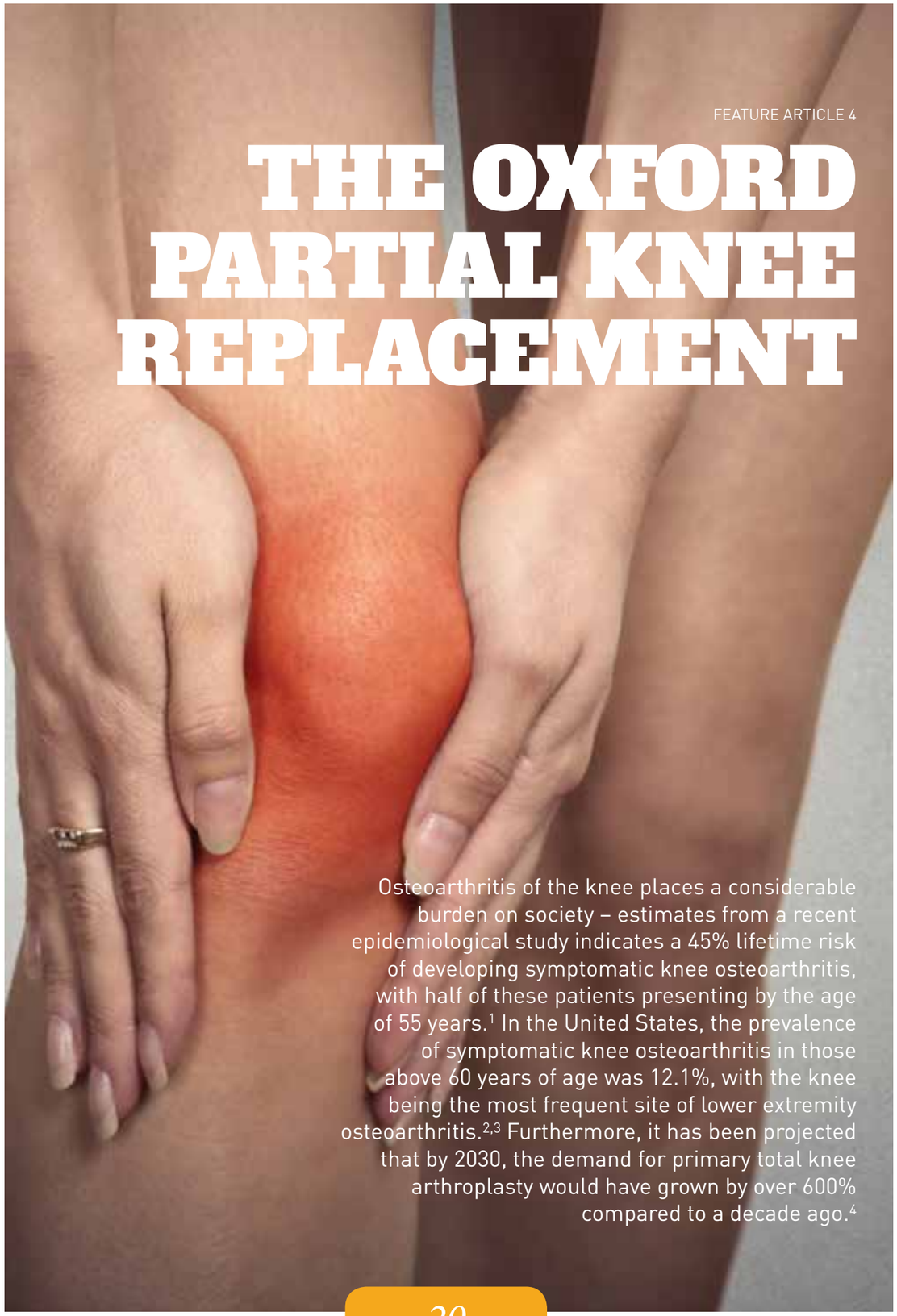
Conclusion

Chronic recurrent dizziness is common and clinicians should try to avoid leaving patients to be stuck with the 'chronic vestibulopathy' or similar label without making efforts to further characterise the condition. Chronic recurrent dizziness can profoundly impact patients' quality of life. Vestibular migraine should be excluded in this group of patients. As with any other chronic disorders, a careful thorough history and examination is necessary for making the correct diagnosis. The symptoms of vestibular migraine can be successfully controlled in the vast majority of patients.

FURTHER READING

1. *Calhoun AH, Ford S, Pruitt AP, Fisher KG. The point prevalence of dizziness or vertigo in migraine--and factors that influence presentation. Headache. 2011;51(9):1388-92.*
2. *Lempert T, Olesen J, Furman J, Waterston J, Seemungal B, Carey J, et al. Vestibular migraine: diagnostic criteria. J Vestib Res. 2012;22(4):167-72.*
3. *Vukovic V, Plavec D, Galinovic I, Lovrencic-Huzjan A, Budisic M, Demarin V. Prevalence of vertigo, dizziness, and migrainous vertigo in patients with migraine. Headache. 2007;47(10):1427-35.*
4. *Eggers SD, Staab JP, Neff BA, Goulson AM, Carlson ML, Shepard NT. Investigation of the coherence of definite and probable vestibular migraine as distinct clinical entities. Otol Neurotol. 2011;32(7):1144-51.*
5. *Zhao JG, Piccirillo JF, Spitznagel EL, Jr., Kallogjeri D, Goebel JA. Predictive capability of historical data for diagnosis of dizziness. Otol Neurotol. 2011;32(2):284-90.*

DR HO EU CHIN
is a consultant in the Department of Otorhinolaryngology, Tan Tock Seng Hospital.



FEATURE ARTICLE 4

THE OXFORD PARTIAL KNEE REPLACEMENT

Osteoarthritis of the knee places a considerable burden on society – estimates from a recent epidemiological study indicates a 45% lifetime risk of developing symptomatic knee osteoarthritis, with half of these patients presenting by the age of 55 years.[1] In the United States, the prevalence of symptomatic knee osteoarthritis in those above 60 years of age was 12.1%, with the knee being the most frequent site of lower extremity osteoarthritis.[2,3] Furthermore, it has been projected that by 2030, the demand for primary total knee arthroplasty would have grown by over 600% compared to a decade ago.[4]

Consequently, it is imperative that patients have access to treatment that relieves their symptoms, facilitates a swift return to normal daily activities, and enhances their quality of life. At the same time, the treatment must have a minimal risk of death and major complications. Currently, there are two treatment modalities that fulfil these stringent criteria – total knee arthroplasty (TKA) and unicompartmental knee arthroplasty (UKA). In UKA procedures, only the arthritic compartment of the knee joint is replaced by a prosthesis (hence the moniker "partial knee replacement"), while TKA typically results in replacement of the entire knee joint (figure 1).

In Singapore, TKA has traditionally been sine qua non in the successful management of patients with symptomatic medial knee arthritis. However, as our understanding of proper patient selection has evolved in tandem with improvements in surgical technique, UKA has emerged as an appealing alternative that provides unique and significant advantages over conventional TKA.

Partial knee replacement – Is it safer and more efficacious compared to total knee arthroplasty?

Compared to TKA, UKA has the technical advantages of a shorter minimally-invasive skin incision, less iatrogenic injury to the soft tissues, minimal disruption of the knee extensor mechanism, and more natural knee kinematics owing to the preservation of all the major knee ligaments (figures 2 and 3). These technical advantages are thought to translate into improved safety, faster post-operative recovery, and superior functional outcomes. Additionally, it is a notable advantage that a UKA is generally much easier to revise than a TKA in the event of implant failure.

Indeed, recent large studies have shown that UKA may well be the safer procedure. A matched study comparing UKA and TKA in over 100,000 knee arthroplasties, using data from the United Kingdom National Joint Registry (UK NJR), found several key

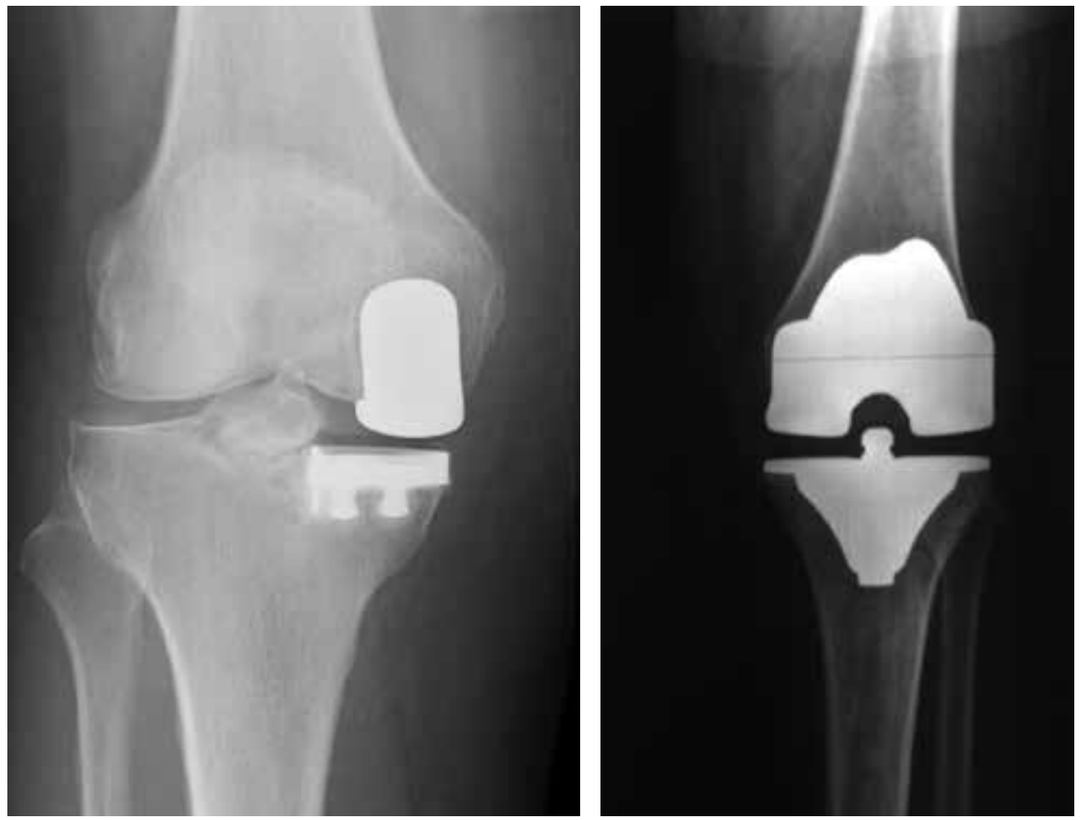


Figure 1. Unicompartmental knee arthroplasty (left), total knee arthroplasty (right).
Image: Fpjacquot under GNU Free Documentation License, Version 1.2.

In the Far East, a recent Japanese study of more than 1,000 Oxford UKAs established a 10-year survival rate of 95%, and concluded that good clinical results were achievable in Asia provided inclusion criteria were followed.

advantages favouring UKA.[5] Mortality rates were significantly lower for UKA (hazard ratio of 0.23 at 30 days, 0.47 at 90 days, 0.69 at 1 year, and 0.85 at 8 years). Intra-operative complications were lower for UKA (OR 0.70, p=0.001), fewer blood transfusions were required (OR 0.18, p<0.001), and the mean length of stay was 1.38 days shorter (p<0.001). Lastly, major post-operative complications were significantly lower in patients undergoing UKA, which included thromboembolism (OR 0.42, p<0.001), stroke (OR 0.28, p=0.002), and myocardial infarction (OR 0.32, p<0.001).

Similarly, Swedish joint registry data showed that, after adjusting for age, gender and year of operation, UKA patients had a two-day shorter hospital stay and fewer serious complications than TKA patients.[6] Also, the Swedish registry found that UKAs were associated with a 2.6 times lower risk of re-operation for infection compared with TKAs.

The UK NJR and Swedish registry data were corroborated by findings from a US multi-centre analysis of 2,235 TKAs versus 605 UKAs over 5 years, which showed overall complication rates of 11.0% for TKA compared to 4.3% for UKA (p<0.0001).[7] In addition, the study showed that TKA was associated with significantly increased rates of transfusion (OR 8.5, p=0.036), ICU admission (OR 7.4, p=0.049), joint manipulation (OR 13.0, p<0.0001), and longer hospital stays (mean 3.3 versus 2.0 days, p<0.0001).

Functional outcomes, as measured with patient-reported outcome measures (PROMs), also favour UKA in the early post-operative period. Data from the New Zealand Joint Registry has shown that,

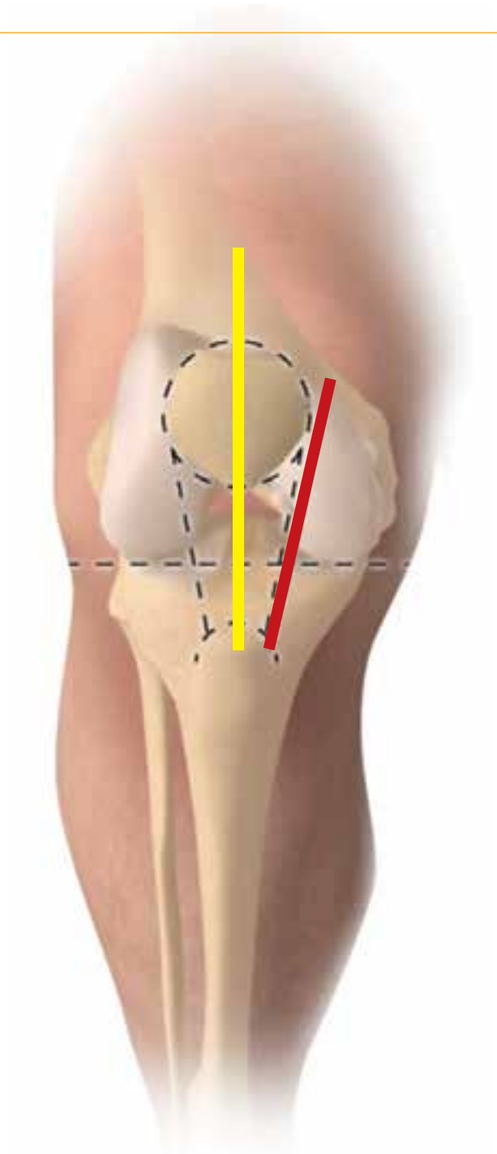


Figure 2. A typical Oxford unicompartmental knee arthroplasty incision (red) is less invasive than that of a total knee arthroplasty incision (yellow).
Image reproduced with permission from Zimmer Biomet.

using the Oxford Knee Score (OKS) at 6 months post-operatively, UKA has more excellent and fewer poor results than TKA.[8] In another matched study from the UK NJR of over 14,000 patients that compared the PROMs between UKA and TKA, the OKS was significantly better with UKA, with more patients achieving an excellent OKS score (OR 1.59, p<0.001).[9]

Hence, the current literature clearly posits that UKA is associated with swifter post-operative recovery and shorter length of hospitalisation, lower mortality and morbidity, and better early functional outcomes.

The case for the Oxford partial knee replacement

UKA prostheses can be divided into fixed-bearing and mobile-bearing designs. Conventionally, one of the major drawbacks of UKA has been the stringent patient selection criteria as established by Kozinn and Scott.[10] This set of criteria was developed based on the authors' experience with fixed-bearing UKA designs, in an effort to decrease implant wear rates and failure. When applying their criteria (which excludes patients under 60 years of age, high activity levels, obesity, and patellofemoral joint arthritis), only 5-10% of patients with symptomatic medial knee arthritis are suitable for UKA.[11-13]

This has two major implications for fixed-bearing UKA prostheses. First, only a small subset of patients can benefit from the advantages inherent to UKA; and second, the typical orthopaedic surgeon will experience significant difficulty in generating sufficient case numbers to maintain surgical proficiency, with predictably detrimental effects on implant survivorship and increased rates of revision surgery.

This is borne out by data from the UK NJR, which shows that the most common number of UKAs implanted per surgeon per year is one, and the next most common number is two, with the mean number being five.[14] When this was compared against revision rates, it was shown that surgeons doing small numbers had a very high revision rate.[15] UKA revision rates dropped steeply until the caseload reached ten cases per year. Perhaps more importantly, it was also shown that surgeons doing more than 30 UKAs per year had a revision rate that was not statistically different from that of TKA (figure 4).

Nonetheless, it is not generally feasible for surgeons to increase the size of their knee arthroplasty practice in order to generate the numbers needed for optimal UKA outcomes. The most expedient way around this obstacle would be to broaden the indications for performing UKAs, which would also allow a larger proportion of patients with symptomatic medial knee arthritis to benefit from UKA, whilst maintaining patient safety and good outcomes. It is with this in mind, perhaps, that the Oxford UKA may make a pivotal difference.

The Oxford UKA prosthesis was developed in 1974 by John Goodfellow and John O'Connor, featuring a unique fully congruent mobile-bearing meniscal insert, which is designed to decrease the wear rate of the implant compared to fixed-bearing prostheses

Figure 3. Left – Anterior & posterior cruciate ligaments (blue) are preserved in unicompartmental knee arthroplasty, together with the uninvolved compartments of the knee; Right – Cruciate-sacrificing total knee arthroplasty prosthesis.
Image reproduced with permission from Zimmer Biomet.

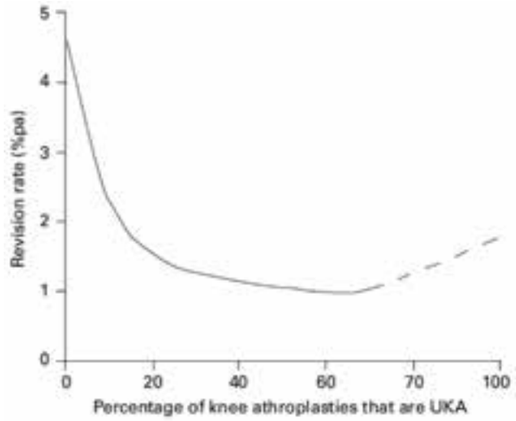


Figure 4. Graph showing the relationship between revision rates and UKA usage (based on data from the UK National Joint Registry). Source: Murray et al. 2015[30]

and simulate normal knee kinematics (figure 5). It is also the only partial knee implant that has good clinically proven survivorship at up to 15 and 20 years.[16-18]

Clinical research has provided strong evidence that the main indication for the Oxford mobile-bearing UKA is anteromedial knee osteoarthritis (AMOA), and that the other Kozinn and Scott contraindications do not apply.[19] AMOA is a pathological condition that has four clearly-defined requirements: 1) bone-on-bone medial osteoarthritis, 2) intact cartilage laterally, 3) functionally intact anterior cruciate ligament, and 4) functionally intact medial collateral ligament. Significantly, when using this set of criteria, the Oxford mobile-bearing UKA can be used safely in up to 50% of patients with symptomatic medial knee osteoarthritis.[20] This would allow most arthroplasty surgeons to exceed 30 Oxford UKAs per year and achieve revision rates that are similar to TKA. When adhering to the AMOA indication, a 10-year survival rate of 98% and 15-year survival rate of 91% was achieved by the designer surgeons.[21,22] This survivorship data was supported by a published 10-year survival rate of 90-99% by non-designer surgeons.[23-27]

In the Far East, a recent Japanese study of more than 1,000 Oxford UKAs established a 10-year survival rate of 95%, and concluded that good clinical results were achievable in Asia provided inclusion criteria were followed.[28] Likewise, a study of 400 Oxford UKAs in Korean patients showed a 10-year survival rate of 94%, and concluded that minimally-invasive Oxford UKA can yield satisfactory clinical and functional outcomes.[29] These studies provide evidence that excellent outcomes can be obtained in Asian patients despite differences in physical morphology and cultural customs.

Conclusion

When treating patients with symptomatic knee osteoarthritis, UKA has several notable advantages over TKA, which include significantly lower mortality risks, lower intra-operative and post-operative complication rates, shorter length of hospitalisation, and superior functional outcomes. However, the criticism directed at UKA has classically centred around higher rates of revision surgery and narrow patient selection.

The Oxford UKA, being a mobile-bearing prosthesis with lower wear rates, can safely be implanted in patients who would traditionally have been considered unsuitable for fixed-bearing UKA designs. The clinically-proven AMOA patient selection criterion is specific to the Oxford UKA prosthesis, and when compared to the Kozinn and Scott criteria for fixed-bearing designs, allows five to ten times more patients to benefit from the advantages of UKA.

Furthermore, multiple large well-designed studies of the Oxford UKA have established a good 10-year prosthesis survivorship of 90-99% in both Western and Far Eastern populations, which is equivalent to the survivorship of most well-performing modern TKA implants. As such, in the hands of experienced surgeons and with proper patient selection, it has been established that there is no significant difference in surgical revision rates when comparing the Oxford UKA against TKA.

Figure 5. The mobile-bearing Oxford Partial Knee implant.
Image reproduced with permission from Zimmer Biomet.

In summary, the mobile-bearing Oxford UKA, which successfully incorporates the benefits inherent to UKA prostheses whilst addressing the traditional drawbacks attributed to fixed-bearing designs, is increasingly recognised as the gold standard treatment for patients with symptomatic anteromedial osteoarthritis of the knee.

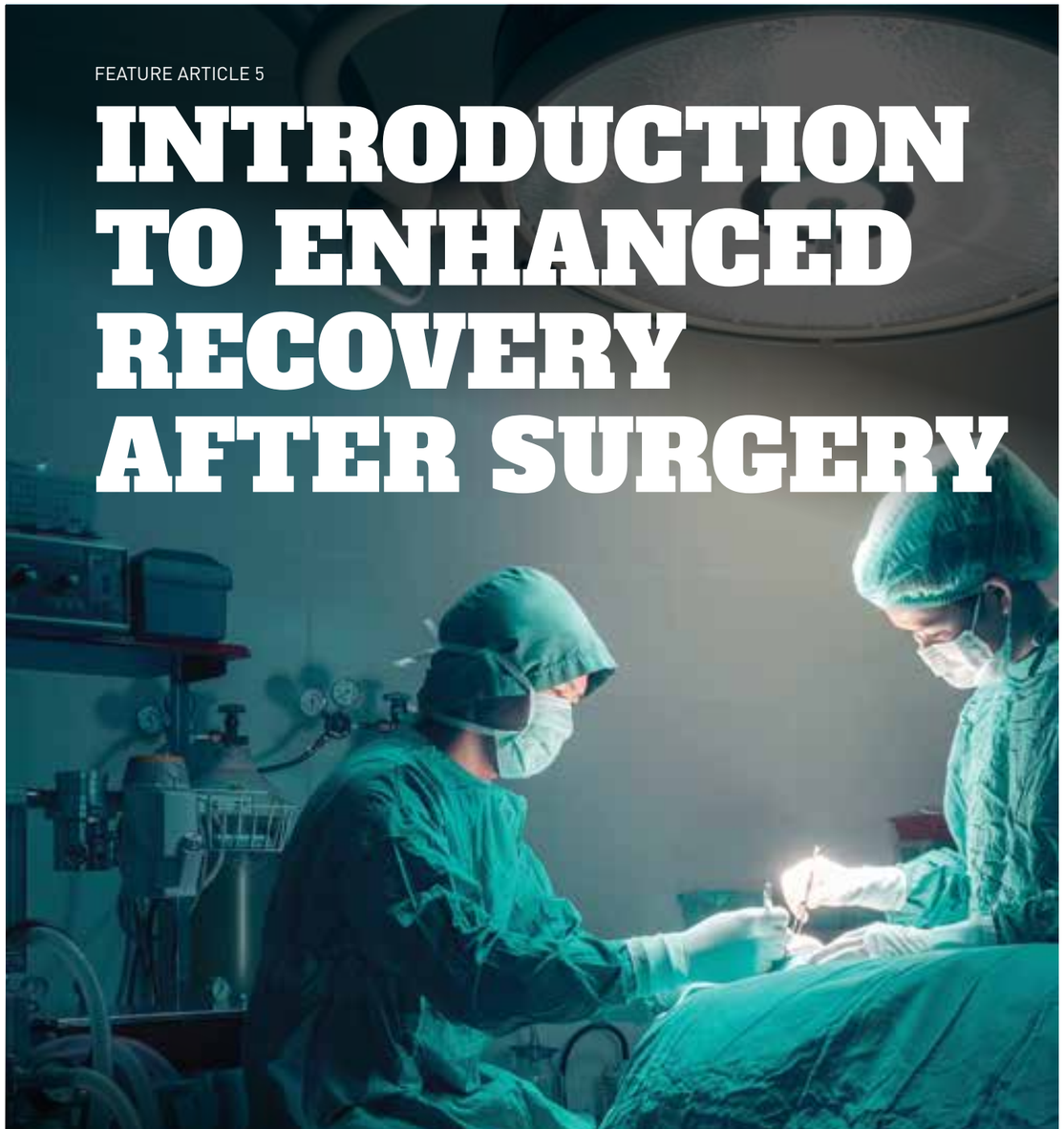
REFERENCES

1. *Murphy L, Schwartz TA, Helmick CG, et al. Lifetime risk of symptomatic knee osteoarthritis. Arthritis Rheum 2008;59:1207–1213.*
2. *Oliveria SA, Felson DT, Reed JI, Cirillo PA, Walker AM. Incidence of symptomatic hand, hip, and knee osteoarthritis among patients in a health maintenance organization. Arthritis Rheum. 1995; 38:1134–41.*
3. *Dillon CF, Rasch EK, Gu Q, Hirsch R. Prevalence of knee osteoarthritis in the United States: arthritis data from the Third National Health and Nutrition Examination Survey 1991–94. J Rheumatol 2006; 33:2271–9.*
4. *Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg [Am] 2007;89-B:780–785.*
5. *Liddle AD, Judge A, Pandit H, Murray DW. Adverse outcomes after total and unicompartmental knee replacement in 101,330 matched patients: a study of data from the National Joint Registry for England and Wales. Lancet 2014;384:1437–1445.*
6. *Robertsson O, Borgquist L, Knutson K, Lewold S, Lidgren L. Use of unicompartmental instead of tricompartmental prostheses for unicompartmental arthrosis in the knee is a cost-effective alternative. 15,437 primary tricompartmental prostheses were compared with 10,624 primary medial or lateral unicompartmental prostheses. Acta Orthop Scand 1999;70(2):170–5*
7. *Brown NM, Sheth NP, Davis K, Berend ME, Lombardi AV, Berend KR, Della Valle CJ. Total knee arthroplasty has higher postoperative morbidity than unicompartmental knee arthroplasty: a multicenter analysis. J Arthroplasty 2012;27(8 Suppl):86-90.*
8. *Fifteen Year Report. January 1999 to December 2013. The New Zealand Joint Registry.*
9. *Liddle AD, Pandit H, Judge A, Murray DW. Patient reported outcomes following total and unicompartmental knee replacement: a study of 14,076 matched patients from the National Joint Register for England and Wales. Bone Joint J 2015;97-B:793–801.*
10. *Kozinn SC, Scott R. Unicondylar knee arthroplasty. J Bone Joint Surg [Am] 1989;71-A:145–150.*
11. *Stern SH, Becker MW, Insall JN. Unicondylar knee arthroplasty. An evaluation of selection criteria. Clin Orthop Relat Res 1993;(286):143-8.*
12. *Riddle DL, Jiranek WA, McGlynn FJ. Yearly incidence of unicompartmental knee arthroplasty in the United States. J Arthroplasty 2008;23(3):408.*
13. *Annual Report 2014 Australian Hip and Knee Arthroplasty Register. 2014.*
14. *10th Annual Report of the National Joint Registry for England, Wales and Northern Ireland. National Joint Registry.*
15. *Liddle AD, Pandit H, Judge A, Murray DW. The effect of surgical caseload on revision rate following total and unicompartmental knee replacement. J Bone Joint Surg Am 2016 Jan 6;98(1):1-8.*
16. *Price AJ, Svard U. A second decade lifetable survival analysis of the Oxford unicompartmental knee arthroplasty. Clin Orthop Relat Res 2011;469(1):174-9.*
17. *Price AJ, Waite JC, Svard U. Long-term clinical results of the medial Oxford unicompartmental knee arthroplasty. Clin Orthop Relat Res 2005;(435):171-80.*
18. *Mercier N, Wimsey S, Saragaglia D. Long-term clinical results of the Oxford medial unicompartmental knee arthroplasty. Int Orthop 2010;34(8):1137-43.*
19. *Pandit H, Jenkins C, Gill HS, et al. Unnecessary contraindications for mobile-bearing unicompartmental knee replacement. J Bone Joint Surg [Br] 2011;93-B:622–628.*
20. *Liddle AD, Pandit H, Judge A, Murray DW. Optimizing Outcomes Following Unicompartmental Knee Replacement: Insights from a Study of 25,982 Cases (Scientific Exhibit SE11) [abstract]. American Academy of Orthopaedic Surgeons Annual Meeting, 2015.*
21. *Murray DW, Goodfellow JW, O'Connor JJ. The Oxford medial unicompartmental arthroplasty: a ten-year survival study. J Bone Joint Surg Br 1998;80:983.*
22. *Pandit H, Hamilton TW, Jenkins C, Mellon SJ, Dodd CA, Murray DW. The clinical outcome of minimally invasive Phase 3 Oxford unicompartmental knee arthroplasty: a 15-year follow-up of 1000 UKAs. Bone Joint J 2015;97-B(11):1493-500.*
23. *Emerson Jr RH, Higgins LL. Unicompartmental knee arthroplasty with the Oxford prosthesis in patients with medial compartment arthritis. J Bone Joint Surg Am 2008;90:118.*
24. *Keys GW, Ul-Abiddin Z, Toh EM. Analysis of first forty Oxford medial unicompartmental knee replacement from a small district hospital in UK. Knee 2004;11:375.*
25. *Rajasekhar C, Das S, Smith A. Unicompartmental knee arthroplasty. 2- to 12-year results in a community hospital. J Bone Joint Surg Br 2004;86:983.*
26. *Svard UC, Price AJ. Oxford medial unicompartmental knee arthroplasty. A survival analysis of an independent series. J Bone Joint Surg Br 2001;83:191.*
27. *Vorlat P, Putzeys G, Cottenie D, et al. The Oxford unicompartmental knee prosthesis: an independent 10-year survival analysis. Knee Surg Sports Traumatol Arthrosc 2006;14:40.*
28. *Yoshida K, Tada M, Yoshida H, Takei S, Fukuoka S, Nakamura H. Oxford phase 3 unicompartmental knee arthroplasty in Japan--clinical results in greater than one thousand cases over ten years. J Arthroplasty. 2013;28(9 Suppl):168-71.*
29. *Lim HC, Bae JH, Song SH, Kim SJ. Oxford phase 3 unicompartmental knee replacement in Korean patients. J Bone Joint Surg Br 2012;94(8):1071-6.*
30. *Murray DW, Liddle AD, Dodd CAF, Pandit H. Unicompartmental knee arthroplasty: is the glass half full or half empty? Bone Joint J 2015;97-B(10 Supple A):3-8.*

DR JAMES WEE LIANG HAO
is a consultant in the Department of Orthopaedic Surgery, Tan Tock Seng Hospital.

FEATURE ARTICLE 5

INTRODUCTION TO ENHANCED RECOVERY AFTER SURGERY



Enhanced Recovery After Surgery (ERAS) represents a paradigm shift from traditional perioperative care to the use of evidenced-based, multimodal, multidisciplinary perioperative pathways. The goal of the ERAS programme is to improve the quality of recovery for patients after surgery. Meta-analyses of randomised controlled trials on ERAS compared to traditional care have consistently shown a reduction in length of stay by 30% and in complication rates by 40%. Compliance to the ERAS recommendations has also demonstrated a "dose-dependent" relationship with outcomes, with compliance levels above 70% associated with better results.

Some of the differences between traditional care and ERAS are highlighted in table 1:

	Traditional care	ERAS programme
Before surgery	Bowel preparation Fasting from midnight	No bowel preparation Clear fluids/carbohydrate drink 2 hours before
During surgery	Liberal intravenous fluids Routine use of nasogastric tubes and drains	Guided intravenous fluid therapy Avoidance of nasogastric tubes and drains
After surgery	Complete rest in bed for days Fasted until bowel functions Opioids for pain relief	Sit out and walk hours after surgery Eat and drink hours after surgery Multimodal opioid-sparing analgesia techniques

Table 1. Traditional care vs ERAS care model

The first ERAS protocol was published in 2005 for colonic resection. Since then, the ERAS principles have been applied to multiple other subspecialties, leading to the development of protocols specific to upper gastrointestinal, hepatobiliary, urological and orthopaedic surgery.

How does ERAS work?

A patient's reaction to surgical stress is the neurohumoral and immunological response to injury, encompassing haematological, immunological and endocrine responses. The extent of these changes is related to the degree of tissue injury, which can be amplified by post-operative complications. Disruption of metabolic homeostasis leads to insulin resistance, tipping the balance towards a catabolic state of glucose and protein metabolism, resulting in hyperglycaemia and protein loss. The patient loses lean muscle mass, the ability to ambulate and has increased risk of respiratory complications, among other changes.[1]

To target this phenomenon, ERAS principally reduces surgical stress and preserves physiological function. The core ERAS components have been proven to be effective in decreasing perioperative stress.

ERAS programme in Tan Tock Seng Hospital

The ERAS® Society was officially registered in 2010 in Stockholm, Sweden, comprising stalwarts in perioperative care from Sweden, the United Kingdom, the Netherlands and Norway. The society was formed after several years of intense discussion and the implementation of consensus protocols in multimodal surgical care.

In 2016, the 1st Asian Australiana and African ERAS® Society Implementation Programme was held in Singapore, with participation from leading centres from the Philippines, Singapore, New Zealand and South Africa.[2]

Tan Tock Seng Hospital implemented the ERAS Programme in March 2016 and we are the first

Figure 1. An overview of the ERAS programme and the ERAS workflow. The ERAS team was awarded with the NHG Team Recognition Awards recently.

of two hospitals in Asia to be recognised by the ERAS® Society as a Centre of Excellence, joining more than 20 other centres around the world. Since the commencement of the programme, more than 250 patients have benefitted from the ERAS care protocol for colorectal surgery. Improvement in outcomes is evident, with reduction of length of stay by 15%, and complications rates by 27%.

Besides establishing an ERAS workflow and recommendations (figure 1), the ERAS Implementation Team has been crucial to the initiation and maintenance of this programme. Our multidisciplinary team consists of surgeons, anaesthetists, nurses, gastroenterologists, dieticians and physiotherapists (figure 2). The team meets fortnightly to review results using the ERAS® Interactive Audit System, and discusses issues and introduces new initiatives to improve the programme.

Colorectal surgery under the ERAS programme

Mechanical bowel preparation was previously prescribed to eliminate solid faecal content and to lower bacterial load. However, with liquefaction of faeces, there is an increased risk of intraoperative spillage. Mechanical bowel preparation also leads to metabolic and electrolyte imbalances, dehydration, fatigue, abdominal pain and bloating, which may have detrimental effects on post-operative recovery.

Meta-analyses of mechanical bowel preparation have not only shown an absence of benefit but an increased incidence of anastomotic leaks and wound infections, resulting in the cessation of its routine use.

Tissue injury leads to the activation of systemic inflammatory response with release of pro-inflammatory cytokines such as interleukins, IL-1 and IL-6. These local changes affect the general inflammatory state as well as on homeostatic, metabolic and circulatory responses.

The more extensive the surgical wound, internal organ manipulation or tissue dissection, the greater the stress and inflammatory response. The inflammatory response first becomes overactive, followed by immune suppression.

Minimally invasive surgery with optimal surgical techniques minimises the total surgical injury. Injury can be primary or secondary. Primary injury is a result of direct trauma to the abdominal wall or organs, or from tissue mobilisation. Secondary or indirect injury occurs because of blood loss and physiological responses to anaesthesia, patient positioning and pneumoperitoneum.

Figure 2. The multidisciplinary ERAS team is made up of members from General Surgery, Dietetics, Gastroenterology, Physiotherapy, Nursing and Anaesthesia.

Laparoscopic techniques can reduce the total additive length of incisions and maximum length of any one incision. Muscle-splitting instead of muscle-dividing techniques and transverse incisions that traverse fewer myotomes and dermatomes can be employed to decrease trauma to the abdominal wall.

The intra-abdominal component of the operation is usually similar, whether performed with open or laparoscopic technique. However, laparoscopic surgery is associated with a reduction in the extent of peritoneal injury, blood loss and formation of adhesions. This may be because laparoscopic technique is characterised by careful and precise dissection within bloodless tissue planes, thereby reducing collateral injury and stimulation.

Benefits of minimally invasive surgery are further enhanced with earlier recovery of bowel function and less postoperative pain, resulting in earlier enteral feeding and mobilisation respectively.

The benefits of minimally invasive surgery, however, have to be balanced with the use of carbon dioxide pneumoperitoneum and non-physiologic patient positioning, which may have detrimental effects, especially in prolonged operations.

The causes of postoperative ileus are often multifactorial, including increased age, male gender, low pre-operative serum albumin, opioid use, long duration of surgery, blood loss, and salt and fluid overload. These factors increase inflammation and oedema, resulting in reduced smooth muscle contractility and ileus.

The causes of postoperative ileus are often multifactorial, including increased age, male gender, low pre-operative serum albumin, opioid use, long duration of surgery, blood loss, and salt and fluid overload. These factors increase inflammation and oedema, resulting in reduced smooth muscle contractility and ileus. Thus, various aspects of ERAS care are designed to mitigate these contributing factors so as to decrease ileus rates.

Chewing gum has been shown to be useful for its cephalo-vagal stimulatory effects, leading to increased gastric motility, and reduced inhibitory inputs from the sympathetic nervous system. Meta-analyses of several small studies have shown that it reduces time to passing flatus and time to first bowel movement. This is a potential addition to our local practice to improve recovery.

Nutrition

Nutrition plays an important role in optimising and enhancing postoperative recovery. Inadequate nutrition, particularly for cancer patients undergoing surgery, is associated with an increased risk of postoperative complications such as delayed wound healing and infectious complications.

Therefore, by correcting nutritional deficits and optimising nutritional status and body weight prior to surgery, recovery times and outcomes can be improved.

Key components of nutrition optimisation for ERAS patients include the identification of patients who are at high nutritional risk for preoperative counselling and avoidance of prolonged perioperative fasting.

Nutrition screening and preoperative optimisation

Nutrition screening is a process to identify an individual who is at high nutritional risk and to determine if a detailed nutrition assessment is indicated. A nutrition screening tool is used to assess patients. The tool assesses a patient's physical appearance (as BMI is not always available), recent food intake and recent weight loss. Losing weight too rapidly prior to surgery can be detrimental to recovery. Hence, for a patient who has difficulty eating or is losing weight, a preoperative referral to the dietician for nutrition optimisation should be considered.

Eating well before surgery is important. A healthy, well balanced diet including a variety of food (from all food groups – rice and meat and their alternatives, fruits and vegetables) is essential for maintenance of immunity and in aiding recovery.

Carbohydrate Loading and Fasting Times

Surgical stress, in the presence of fasting, worsens the catabolic state. Insulin resistance is a compensatory mechanism during starvation and is mediated by inhibition of glucose oxidation. It is associated with increased protein catabolism. For the perioperative patient, this evolutionary compensatory mechanism leads to delayed recovery.

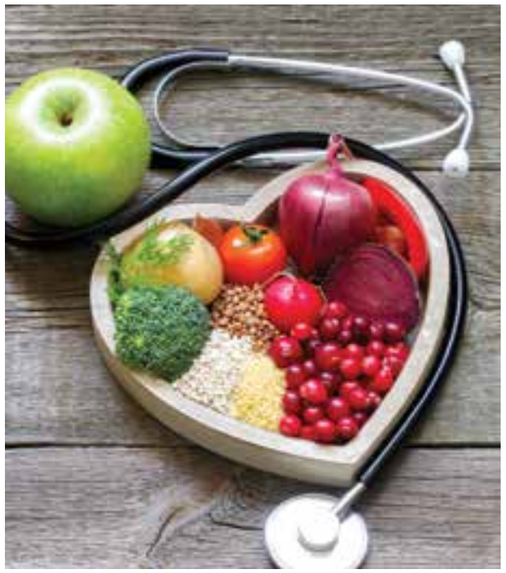
Preoperative carbohydrate loading raises insulin sensitivity and this effect persists to the post-operative period, resulting in less insulin resistance. Cellular metabolism shifts to a more anabolic state, with less hyperglycaemia, greater retention of protein, preservation of lean body mass and reduced complications. Thus, clear complex carbohydrate drinks on the night before surgery and 2 hours prior to surgery have been recommended.

Current guidelines for fasting times are about 6 hours for solid food and 2 hours for clear liquids as recommended by both the European[3] and American[4] Societies of Anaesthesia. This is also recognised in the ERAS perioperative guidelines. Meta-analyses of randomised controlled trials show that fasting times of 2-4 hours for clear liquids result in lower gastric volumes with higher pH compared to a fast of more than 4 hours.[4] However, these guidelines do not apply for certain situations such as in emergent surgery or for the patient with high risk of aspiration.

The clear complex carbohydrate drink 2 hours before surgery has been shown to empty predictably from the stomach by the time of surgery.[5] Nevertheless, aspiration risk remains a concern in patients with risk factors for delayed gastric emptying such as poorly controlled diabetes. Longer fasting times may be required for these patients and is usually decided during the pre-anaesthetic evaluation.

Postoperative nutrition

Early introduction of fluid and food after surgery has been shown to reduce the risk of infection and shorten the length of stay, with no increase in risk of anastomotic dehiscence in colorectal surgery.[6,7] This begins as early as on the day of surgery when the patient is given oral nutritional supplement drinks. These supplements are complete and balanced in nutrition, providing macronutrients and micronutrients to optimise the patient's nutritional status in order to meet their increased needs during recovery.



Immunonutrition

In addition to the physiological and metabolic stress response, surgery leads to a pro-inflammatory followed by an immunosuppressed state. The potential to modulate the activity of the immune system by interventions with specific nutrients (arginine, omega-3 fatty acids and nucleotides) is the underpinning of immunonutrition. Use of these supplements in elective gastrointestinal surgical patients can contribute to improvement in outcomes including reduction in infectious complications, improved wound healing and reduced length of stay.

Patients with suboptimal nutritional status prior to surgery are prescribed a specially formulated supplement for 5 days before surgery to augment their nutrition.

Prehabilitation

Besides the nutritional status, the functional status of a perioperative patient also often requires optimisation. This is imperative to mitigate the effects of the impending surgical stress and in postoperative recovery.

Surgical stress, physical inactivity, fasting and psychological distress represent major stressors to the body. The major stressors adversely affect the short- and long-term capacity to perform activities of daily living and the overall quality of life.

Major surgery is associated with a 40% reduction in functional capacity. The elderly, the oncology patients, and those with limited protein reserves are most susceptible to the negative effects of surgery. Traditionally, physical interventions involve only the postoperative period. However, this may not be the most opportune time to introduce these as many postoperative patients are unwilling to engage in physical therapy, thinking that the activity could affect wound healing. Many of these patients may also have to contend with the emotional and psychological impact of the oncological diagnosis.

The preoperative period is thought to be a more appropriate time to introduce some of these measures that contribute to recovery. Patients can be actively engaged in the preparation process of improving their physical status, which could aid in alleviating emotional stress surrounding the surgery.

"Prehabilitation" is an intervention designed to improve functional capacity in anticipation of an upcoming surgical stressor. It has been postulated that a prehabilitation intervention in the preoperative period can raise the patient's physical status, thereby mitigating the detrimental effects of surgery on their functional capacity and resulting in an earlier return to normal function.

In 2002, Ditmyer[8] and Topp[9] and colleagues proposed that patients who receive an exercise programme before surgery recover more rapidly compared with patients who remained sedentary. Since then, several studies have been performed, using various exercise programmes.

The first systematic review of reasonable methodological quality that studied 12 studies was published in 2011.[10] Preoperative exercise therapy was shown to reduce postoperative complication rates and accelerate discharge from hospital in patients undergoing cardiac and abdominal surgery.

How does Prehabilitation Benefit Patients?

When exercise is undertaken on a regular basis, the body becomes more efficient in its adaptation to the stress of exercise. Organ systems such as the cardiovascular, respiratory, musculoskeletal, neurological, and endocrine systems become more adept at the anticipation of and the compensation for each bout of exercise. Trained individuals are able to exploit a greater percentage of their functional range, or maximal physiologic capacity, during periods of physical stress. For example, if a sedentary person runs to catch a bus, his body, being not accustomed to performing this level of activity, is able to use only a small proportion of its potential functional capacity, resulting in a limited ability to meet that particular demand. This person will develop a rapid heart rate, sweating, a feeling of discomfort and breathlessness, and he might be unable to speak with the bus driver or climb the stairs in the vehicle. In contrast, a person who exercises regularly is better able to cope with the stress by harnessing a greater proportion of his physiologic reserve. Although he runs the same distance, his body is better able to handle the bout of activity.

Physiologic reserve is the overall range of functional capacity in an individual, determined by genetics, and includes all organ systems in the human body. Ageing decreases the physiologic reserve and this deterioration begins in early adulthood. Although the ageing process itself compromises the physiologic reserve, the effects are compounded by sedentary lifestyles. Regular physical exercise can attenuate the degree of physical decline associated with ageing.

Functional capacity, as determined by cardiopulmonary exercise testing, has been associated with surgical outcomes in non-cardiac surgery.[10] Patients who are less fit have a higher incidence of postsurgical morbidity and mortality. The goal of prehabilitation is to improve fitness, including flexibility, to optimise postoperative recovery and maintain physical function.

How to Exercise?

Engaging and encouraging a patient to do as much as they can in the period that is available before surgery may be the most efficient and effective approach. This strategy is especially important for the patient who has been previously sedentary. Exercise programmes for prehabilitation should introduce exercise that is greater than the individual's current level of activity but not overly intense. This enables the whole system to experience the stress of additional work but at the same time avoid fatigue and injury.

Prehabilitation over a four-week period has been shown to be sufficient in improving distance walked in the six-minute walk test, decreasing heart rate and oxygen consumption at submaximal workloads, and improving peak power output.[11] The programme should consist of both aerobic and muscle strengthening exercises. Allowing adequate rest between sessions of exercise is also important, to recover physically and to reap the physiological benefits from the session. Physical improvement is attained with gradual increase of exercise intensity.

In general, individuals who are the least fit and the most sedentary show the most improvement when they commence an exercise programme. Since the ratio of actual physiologic reserve to total

physiologic reserve is low, even small amounts of physical training can lead to marked improvement.

Patients compliant to simple walking and breathing exercise recommendations have been shown to make marked improvements in walking capacity, as measured by the six-minute walk test. The elderly postsurgical patients often decline more rapidly with enforced bed rest and physical inactivity because of their preexisting low functional capacity, thus this group is likely to benefit from a targeted intervention. In addition, prehabilitation programmes that are multimodal (including physical, nutritional and psychological components) seem to be more effective than those that are unimodal.

In a recent pilot study, a multimodal prehabilitation programme comprising moderate-intensity physical exercise, nutritional counselling, protein supplementation and anxiety-reducing strategies within the context of the ERAS protocol revealed that more than 80% of patients with cancer undergoing colorectal resection were able to return to preoperative functional capacity by 8 weeks, compared to 40% in a control group without the prehabilitation programme.[12]

Nursing support is a key pillar in the successful implementation and maintenance of any workflow. Instead of a dedicated ERAS nurse coordinator which many institutions employ, we depend on several key nurses of the ERAS workgroup to see a patient through his journey from pre-surgery counselling to follow-up after discharge.

Nursing and ERAS

From optimisation of nutritional and physical statuses preoperatively to follow-up post-discharge, data collection and data analysis, nurses are crucial in every step of the ERAS programme.

Nursing support is a key pillar in the successful implementation and maintenance of any workflow. Instead of a dedicated ERAS nurse coordinator which many institutions employ, we depend on several key nurses of the ERAS workgroup to see a patient through his journey from pre-surgery counselling to follow-up after discharge.

In the Pre-Operative Counselling and Evaluation Clinic, coordination of physiotherapist and dietician appointments are carried out by nurses (figure 3). Patients no longer come for surgery without knowing what to expect in the postoperative recovery period. Nurses counsel the patients about preoperative preparation including reinforcing the schedule for oral nutritional supplements and instructions about the medications to be taken on the morning of the surgery, as well as postoperative issues like analgesia modalities, feeding and mobilisation goals. This manages the patients' expectations and improves compliance.

Patients are mobilised after their surgery on the day that they return to the ward. Nursing leads guide other nurses in sitting these patients out in the chair and ensure that oral nutritional supplements are served appropriately. Nursing champions educate and inform their ward colleagues about how they can contribute to this form of well-coordinated, evidence-based care of the surgical patient. From the first postoperative day, after being assessed by the physiotherapist, nurses encourage and assist the patients in ambulation.

Nurses provide educational, emotional and psychological support to the surgical patient not only during the inpatient stay but extend this care to the post-discharge period. Patients are contacted by phone 30 days after they have been discharged, as part of the postoperative follow-up and continuity of care.

The ERAS philosophy is based on team-work, audits and data-driven systemic change. A major role that nurses play is in the collection of reliable audit data. Data on postoperative nausea and vomiting, pain scores, and fluid balance, for examples, are assessed and recorded by nurses. They also ensure that demographic, surgical and anaesthesia data have all been accurately recorded. From mundane logistics to the biopsychosocial care of the patient, nurses play a pivotal role in the ERAS pathway.

Figure 3. The ERAS team of nurses and colleagues from General Surgery, Physiotherapy and Dietetics.

Anaesthesia and ERAS

Tom Burton, co-founder of Health Catalyst, an American data warehouse, analytics and outcomes-improvement company, discusses in his article "Data for Improving Healthcare vs Data for Exasperating Healthcare Workers" the approach to systemic improvement by reducing variability.[13] This focused effort on meeting the evidence-based baseline standards of care leads to an overall improvement in outcomes.

Similarly, perioperative care of the patient undergoing surgery under the ERAS pathway is standardised, including the various aspects of care provided by the anaesthetist.

Previously, perioperative benzodiazepines may be given routinely and often patients are loaded with intravenous fluid at induction to avoid hypotension. With the paradigm shift to focusing on the three central tenets of ERAS: mitigating the perioperative stress response to surgery, facilitating early mobilisation and enabling early feeding, these routine practices are viewed as detrimental rather than beneficial. Furthermore, patients are no longer fasted for hours before surgery and thereby are euvolemic on arrival in the operating theatre, therefore omitting the need for fluid-loading.

Perioperative medicine has long been an area helmed by the anaesthetists. Through working in a multi-disciplinary ERAS team, knowledge of preoperative optimisation of a patient's medical conditions is shared among all the members involved in the patient's care, with a common goal of improving care and patient experience. For example, smoking cessation at least 4 weeks prior to surgery can be advised before the patient visits the anaesthetic clinic. Guidelines for ERAS for various surgical specialties are put together by various healthcare providers and include preoperative optimisation of conditions especially those affecting the cardiovascular, renal and respiratory systems.[2]

Perioperative guidelines include both evidence-based and expert-opined best practices. These include thromboprophylaxis (with pneumatic calf compressors or antiembolism stockings), timely antibiotic prophylaxis administration, postoperative nausea and vomiting prophylaxis, prevention of intraoperative hypothermia and maintaining normoglycaemia.

A standardised anaesthetic protocol avoids excessive depth of anaesthesia as this depresses physiological status,[14] delays awakening, and affects cognitive function especially in the elderly.[15] Depth of anaesthesia monitoring such as the bispectral index is often used in susceptible patients to optimise treatment.

Central to anaesthesia practice is fluid therapy and analgesia. Fluid therapy is aimed at maintaining zero-balance. Excessive fluid has been shown to affect anastomotic integrity and contributes to postoperative ileus.[16] A goal-directed approach to fluid therapy is advised using balanced fluids and avoiding the sodium load from 0.9% sodium chloride solutions.

Analgesia choices can influence all three tenets of ERAS. For example, epidural analgesia for open surgery has been shown to minimise insulin

resistance[17] and protein catabolism[16] by decreasing counter-regulatory hormones through its effects on the central and peripheral nervous system.[17] Intraoperative analgesia is always multimodal including paracetamol, non-steroidal anti-inflammatory drugs, lignocaine, ketamine, abdominal blocks and pre-peritoneal local anaesthetic infiltration. Multimodal analgesia aims to minimise opioids, avoiding its undesired effects such as nausea, vomiting, respiratory depression and decreased bowel motility. Multiple factors influence the analgesia regime including the surgical approach, comorbidities and risk-benefit ratio. For example, a recent study demonstrated that intravenous lignocaine infusion provided inferior analgesia to epidural but was associated with improvement in several aspects of recovery including less hypotension and less nausea and vomiting.[18]

The anaesthetist influences many aspects of recovery after surgery and works closely with the surgeon in steering the ERAS team towards improving the quality of recovery and patient outcomes.

Conclusion

Every member of this multifaceted ERAS team is essential in contributing to the success of this perioperative coordinated care. The goal is to achieve the triple aim of decreased cost, better care and better health.

REFERENCES

1. *Scott MJ, Baldini G, Fearon KC, Feldheiser A, Feldman LS, Gan TJ, et al. Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 1: pathophysiological considerations. Acta Anaesthesiol Scand. 2015;59(10):1212-31.*
2. *ERAS Society. ERAS History 2017 [Available from: http://erassociety.org/about/history/.*
3. *Smith I, Kranke P, Murat I, Smith A, O'Sullivan G, Soreide E, et al. Perioperative fasting in adults and children: guidelines from the European Society of Anaesthesiology. Eur J Anaesthesiol. 2011;28(8):556-69.*
4. *Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. Anesthesiology. 2011;114(3):495-511.*
5. *Scott MJ, Fawcett WJ. Oral carbohydrate preload drink for major surgery - the first steps from famine to feast. Anaesthesia. 2014;69(12):1308-13.*
6. *Lieffers JR, Bathe OF, Fassbender K, Winget M, Baracos VE. Sarcopenia is associated with postoperative infection and delayed recovery from colorectal cancer resection surgery. Br J Cancer. 2012;107(6):931-6.*
7. *Evans DC, Martindale RG, Kiraly LN, Jones CM. Nutrition optimization prior to surgery. Nutr Clin Pract. 2014;29(1):10-21.*
8. *Ditmyer MM, Topp R, Pifer M. Prehabilitation in preparation for orthopaedic surgery. Orthop Nurs. 2002;21(5):43-51; quiz 2-4.*
9. *Topp R, Ditmyer M, King K, Doherty K, Hornyak J, 3rd. The effect of bed rest and potential of prehabilitation on patients in the intensive care unit. AACN Clin Issues. 2002;13(2):263-76.*
10. *Valkenet K, van de Port IG, Dronkers JJ, de Vries WR, Lindeman E, Backx FJ. The effects of preoperative exercise therapy on postoperative outcome: a systematic review. Clin Rehabil. 2011;25(2):99-111.*
11. *Li C, Carli F, Lee L, Charlebois P, Stein B, Liberman AS, et al. Impact of a trimodal prehabilitation program on functional recovery after colorectal cancer surgery: a pilot study. Surg Endosc. 2013;27(4):1072-82.*
12. *Carli F, Scheede-Bergdahl C. Prehabilitation to enhance perioperative care. Anesthesiol Clin. 2015;33(1):17-33.*
13. *Burton T. Data for improving healthcare vs data for exasperating healthcare workers 2017 [Available from: http://thehealthcareblog.com/blog/2017/01/29/data-for-improving-healthcare-vs-data-for-exasperating-healthcare-workers/.*
14. *Feldheiser A, Aziz O, Baldini G, Cox BP, Fearon KC, Feldman LS, et al. Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 2: consensus statement for anaesthesia practice. Acta Anaesthesiol Scand. 2016;60(3):289-334.*
15. *Chan MT, Cheng BC, Lee TM, Gin T. BIS-guided anesthesia decreases postoperative delirium and cognitive decline. J Neurosurg Anesthesiol. 2013;25(1):33-42.*
16. *Carli F, Halliday D. Continuous epidural blockade arrests the postoperative decrease in muscle protein fractional synthetic rate in surgical patients. Anesthesiology. 1997;86(5):1033-40.*
17. *Schricker T, Meterissian S, Wykes L, Eberhart L, Lattermann R, Carli F. Postoperative protein sparing with epidural analgesia and hypocaloric dextrose. Ann Surg. 2004;240(5):916-21.*
18. *Terkawi AS, Tsang S, Kazemi A, Morton S, Luo R, Sanders DT, et al. A Clinical Comparison of Intravenous and Epidural Local Anesthetic for Major Abdominal Surgery. Reg Anesth Pain Med. 2016;41(1):28-36.*

FURTHER READING

- *Hennis PJ, Meale PM, Grocott MP. Cardiopulmonary exercise testing for the evaluation of perioperative risk in non-cardiopulmonary surgery. Postgrad Med J. 2011;87(1030):550-7.*
- *Kim DJ, Mayo NE, Carli F, Montgomery DL, Zavorsky GS. Responsive measures to prehabilitation in patients undergoing bowel resection surgery. Tohoku J Exp Med. 2009;217(2):109-15.*
- *Hannemann P, Lassen K, Hausel J, Nimmo S, Ljungqvist O, Nygren J, et al. Patterns in current anaesthesiological peri-operative practice for colonic resections: a survey in five northern-European countries. Acta Anaesthesiol Scand. 2006;50(9):1152-60.*
- *Lewis SJ, Egger M, Sylvester PA, Thomas S. Early enteral feeding versus "nil by mouth" after gastrointestinal surgery: systematic review and meta-analysis of controlled trials. BMJ. 2001;323(7316):773-6.*
- *Han-Geurts IJ, Hop WC, Kok NF, Lim A, Brouwer KJ, Jeekel J. Randomized clinical trial of the impact of early enteral feeding on postoperative ileus and recovery. Br J Surg. 2007;94(5):555-61.*

The authors of this article are:

Front row (left to right):
DR HOW KWANG YEONG *(Consultant, Department of General Surgery and Chairperson of the TTSH ERAS Core Team),* ***DR VERA LIM*** *(Associate Consultant, Department of Anaesthesiology, Intensive Care and Pain Medicine),* ***MS KITTY HO PUI SIM*** *(Nurse Clinician, Pre-admission Assessment, Counselling and Evaluation Clinic),* ***MR JAYACHANDRAN BALACHANDRAN*** *(Principal Physiotherapist, Department of Physiotherapy) and* ***DR JONATHAN TAN*** *(Senior Consultant and Director, Surgical Intensive Care Unit in the Department of Anaesthesiology, Intensive Care and Pain Medicine, and Co-chairperson of the TTSH ERAS Core Team).*

Back row (left to right):
MS ONG YAWEI *(Senior Dietitian, Department of Nutrition & Dietetics),* ***MS KONG LAN PEI*** *(Nurse Clinician and Chair, ERAS Nursing Workgroup) and* ***DR LIU HUIMIN*** *(Associate Consultant, Department of General Surgery).*

OSTEOPOROSIS IN CHRONIC KIDNEY DISEASE: A CLINICAL CONUNDRUM

It is now common to encounter patients suffering from renal impairment and osteoporosis. With a rapidly ageing population in Singapore, healthcare providers will increasingly face the herculean task of managing patients with age-related comorbidities such as osteoporosis and chronic kidney disease (CKD). Both of these conditions increase the susceptibility for fragility fractures but their similarity ends there.[1-2] Their distinct pathophysiologic states present diagnostic and therapeutic challenges for patients with coexistent osteoporosis and CKD.

Diagnosis of osteoporosis

The diagnosis of osteoporosis in CKD stages 4-5 is neither straightforward nor clearly defined, because the bone mineral density (BMD) does not predict fracture risk as it does in the general population or determine the extent of renal osteodystrophy.[3]

For instance, dual energy X-ray absorptiometry (DEXA) is currently the method of choice for measuring BMD to establish or confirm a diagnosis of osteoporosis, assess fracture risk, and monitor efficacy of pharmacological treatment. However, it has limited utility in CKD for diagnosis or risk prediction because it cannot assess alterations in bone microarchitecture or bone turnover moderated by biochemical abnormalities in CKD mineral and bone disorder (CKD-MBD). Hence, while osteoporosis may also be a component of the aberrant bone metabolism observed in severe CKD, CKD-MBD itself may lead to artefactual changes in BMD and result in misdiagnosis.

In addition, the Fracture Risk Assessment Tool (FRAX), introduced by the World Health Organisation in 2008 to estimate the 10-year probability of hip fracture and major osteoporotic fracture, does not include any adjustment of risk according to renal function. Just as fall risk has not been included in the FRAX model, clinicians will need to incorporate renal function into their clinical interpretation of absolute fracture risk when utilising FRAX in patients with renal impairment.[4]

Treatment of osteoporosis

Typical osteoporosis treatment may do more harm than good in patients with impaired renal function. There is a theoretical concern that agents which reduce bone turnover may further increase fracture risk in adynamic renal bone disease, a specific form of renal osteodystrophy characterised by very low bone turnover and increased bone fragility.

As such, the Kidney Disease: Improving Global Outcomes (KDIGO) workgroup has recommended that in patients with CKD stages 3-5D with biochemical abnormalities of CKD-MBD and low BMD and/or fragility fractures, treatment choices should take into account the magnitude and reversibility of the biochemical abnormalities and the progression of CKD, with consideration of a bone biopsy.[3] Most drugs used to treat osteoporosis are contraindicated in patients with CKD stages 4-5 (i.e. eGFR < 30 mL/min/1.73 m^2).

(a) Bisphosphonates

Bisphosphonates are analogues of inorganic pyrophosphate which reduce osteoclast-induced bone resorption. Despite being the current mainstay of osteoporosis therapy, they have traditionally been avoided in CKD because they rely on renal elimination and have not been investigated in clinical trials in patients with osteoporosis and severe CKD.

There have been retrospective analyses reporting increased BMD and fracture prevention regardless of the degree of renal impairment with oral risedronate and alendronate for postmenopausal osteoporosis.[5-6] There is no evidence of renal deterioration or damage in these patients. Though these analyses excluded patients with elevated parathyroid hormone (PTH) levels or other evidence of CKD-MBD, only 7-10% of them had severe renal impairment (creatinine clearance (CrCl) ranging from 15 to 29 mL/min). Hence, data remain limited regarding fracture prevention in those with severe CKD resulting in secondary hyperparathyroidism and end-stage renal failure. A retrospective cohort study in 122,727 patients aged ≥66 years with a fragility fracture (4.1% with severe renal impairment) also found that oral bisphosphonate use was not associated with acute kidney injury.[7]

Bisphosphonates may differ in their risk of nephrotoxicity.[8] Transient elevation in serum creatinine has been reported in patients receiving intravenous ibandronate and zoledronic acid; however, treatment with these agents does not result in long-term renal deterioration or accelerated disease progression.[9-10] In the DIVINE study conducted in postmenopausal women at increased risk for renal disease, both bolus injection and slow infusion of ibandronate showed similar renal safety profiles as that of oral alendronate.[11] In these studies, only a very small proportion of patients (<6%) had severe renal impairment. On the other hand, in August 2010, post-marketing surveillance led the Singapore Health Science Authority to issue a safety alert regarding reports of renal impairment and renal failure associated with the use of intravenous zoledronic acid.[12] The majority of the cases were reported in patients with pre-existing medical conditions or risk factors (advanced age, renal impairment, and concurrent or preceding dehydration) or who had concurrent exposure to nephrotoxic agents. Rare cases of renal failure requiring dialysis or fatal outcomes have been reported in patients with pre-existing renal impairment and concomitant risk factors.

In two small studies of dialysis patients, intravenous ibandronate 2 mg every 4 weeks for 48 weeks improved BMD, and alendronate 35 mg every week for 6 weeks resulted in stabilisation of hip BMD after 6 months compared to the placebo group.[13-14] Although statistically significant, the difference is too small to be clinically meaningful.

In addition to the risk of hypocalcaemia, long-term use of bisphosphonates may excessively suppress bone turnover and reduce repair of microcracks, resulting in bone fragility and fractures. While clinical evidence remains conflicting, bisphosphonates should be avoided when low bone turnover, adynamic bone disease or osteomalacia are present or suspected because of the potential for harm. The use of bisphosphonates may be considered in the subset of patients with severe CKD and low BMD but high bone resorption. However, even in this group, bisphosphonate should be used with caution, because by diminishing bone resorption and causing incremental reductions in levels of serum ionised calcium, the medication may induce hyperparathyroidism over time.

(b) Denosumab

When denosumab was approved for osteoporosis treatment, this anti-RANKL monoclonal antibody generated a false sense of security for its absence of renal elimination, which supposedly gave it an advantage over existing osteoporosis agents.

However, its landmark FREEDOM trial excluded patients with eGFR <30 mL/min. In a post-hoc analysis, there were only 73 women with eGFR of 15 to 29 mL/min and none with eGFR <15 mL/min.[15] As a consequence, while denosumab was shown to improve BMD with safety in patients with CKD, there were too few patients with stage 4 CKD to draw any meaningful conclusions about the efficacy and safety of the drug in those with severe renal impairment.

Like bisphosphonates, denosumab inhibits bone resorption which may induce hypocalcaemia. It also limits bone formation, raising concern about adynamic bone disease. When treated with denosumab, patients with severe renal impairment should be closely monitored as they are predisposed to a higher risk of hypocalcaemia. This was exemplified in a single-dose study of denosumab in patients with renal function ranging from normal to dialysis-dependent kidney failure.[16]

(c) Raloxifene

Raloxifene is a selective oestrogen receptor modulator with less than 6% of the dose eliminated renally. It has been demonstrated to increase BMD and reduce the risk for vertebral fractures in postmenopausal women with osteoporosis.[17] This effect was consistent irrespective of renal function in a post-hoc analysis involving women with age-related CKD. Adverse events were similar within and across each subgroup of renal function. However, only 0.8% of patients had CrCl within the range of 20 to 30 mL/min, and those with elevated PTH levels or low vitamin D levels were excluded.

Treatment with raloxifene 60 mg daily for 1 year in postmenopausal women on haemodialysis with severe osteopenia or osteoporosis was associated with significant improvement in lumbar spine BMD and decreased bone resorption markers.[18] No issues with vascular access or dialysis catheters occurred throughout the study duration, despite concerns over the potential risk of stroke and thromboembolic events.

(d) Teriparatide

Unlike the agents discussed above, teriparatide is a recombinant analogue of human PTH with anabolic properties. Its pivotal trials recruited patients with a serum creatinine ≤177 μmol/L and a normal serum PTH level, hence there is no clinical trial data for patients with CKD stages 4-5 or with evidence of CKD-MBD.

Teriparatide may be a useful option for CKD patients with adynamic bone disease. In a case report, a patient with stage 5 CKD on haemodialysis presented with multiple pain fractures and bone histomorphometry demonstrating low-turnover bone disease. He was given subcutaneous teriparatide 20 mcg daily for 24 months, which improved bone formation. Larger studies are needed to further assess the role of teriparatide in adynamic bone disease.[19]

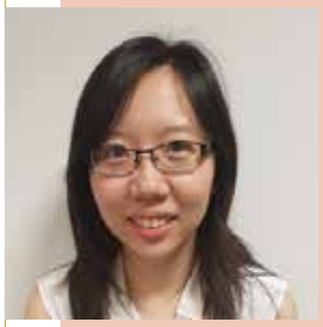
Conclusion

Few data exist for patients with more advanced CKD and/or CKD-MBD. At present, initiation of pharmacologic therapy should only be considered by specialists after CKD-MBD is ruled out, and the risks and benefits thoroughly weighed and discussed with the patient. Until further evidence is available, treatment decisions in these patients will be particularly difficult and remain highly dependent on individual clinician judgment.

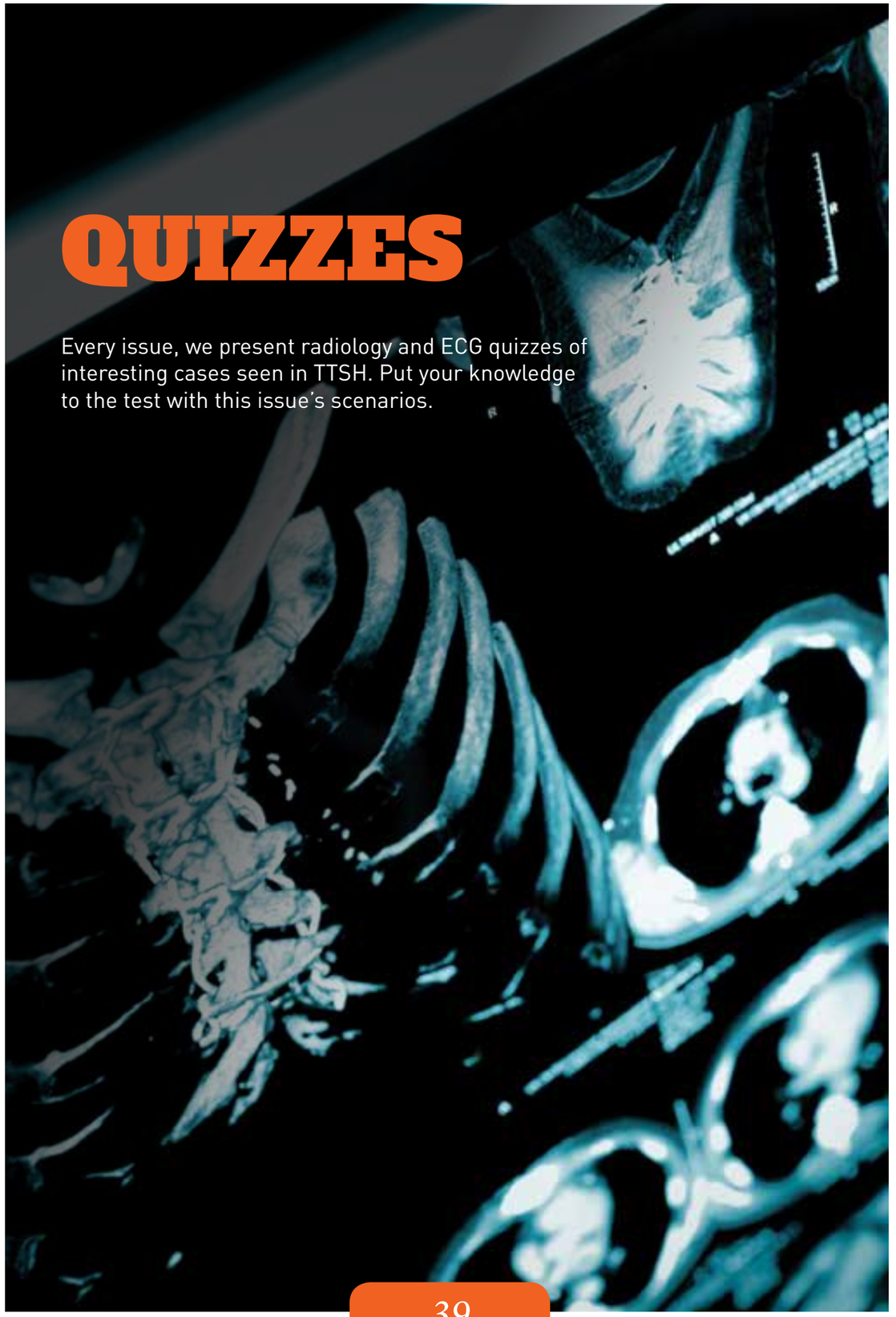
Adequate calcium and vitamin D intake are essential for bone health, but they must be used judiciously to avoid vascular calcification in patients with CKD stages 4-5 who have very low capacity for calcium uptake in the bone compartment. It is also important to ensure that patients do not receive bisphosphonates or denosumab until hypocalcaemia is corrected.

REFERENCES

1. *Ensrud KE, Lui LY, Taylor BC, Ishani A, Shlipak MG, Stone KL, et al. Renal function and risk of hip and vertebral fractures in older women. Arch Intern Med 2007;167(2):133-9.*
2. *Nitsch D, Mylne A, Roderick PJ, Smeeth L, Hubbard R, Fletcher A. Chronic kidney disease and hip fracture-related mortality in older people in the UK. Nephrol Dial Transplant 2009;24(5):1539-44.*
3. *Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD). Kidney Int Suppl 2017;7:1–59.*
4. *Miller PD, Jamal SA, West SL. Bone mineral density in chronic kidney disease use and misuse. Clinical Review in Bone and Mineral Metabolism 2012;10(30):163-73.*
5. *Miller PD, Roux C, Boonen S, Barton IP, Dunlap LE, Burgio DE. Safety and efficacy of risedronate in patients with age-related reduced renal function as estimated by the Cockcroft and Gault method: a pooled analysis of nine clinical trials. J Bone Miner Res 2005; 20:2105–115.*
6. *Jamal SA, Bauer DC, Ensrud KE, Cauley JA, Hochberg M, Ishani A, et al. Alendronate treatment in women with normal to severely impaired renal function: an analysis of the fracture intervention trial. J Bone Miner Res 2007; 22:503–8.*
7. *Shih AW, Weir MA, Clemens KK, Yao Z, Gomes T, Mamdani MM, et al. Oral bisphosphonate use in the elderly is not associated with acute kidney injury. Kidney Int 2012;82:903-8.*
8. *Miller PD, Jamal SA, Evenepoel P, Eastell R, Boonen S. Renal safety in patients treated with bisphosphonates for osteoporosis: a review. J Bone Miner Res 2013;28(10):2049-59.*
9. *Delmas DP, Adami S, Strugala C, Stakkestad JA, Reginster JY, Felsenberg D, et al. Intravenous ibandronate injections in postmenopausal women with osteoporosis: one-year results from the dosing intravenous administration study. Arthritis Rheum 2006;54(6):1838-46.*
10. *Boonen S, Sellmeyer DE, Lippuner K, Orlov-Morozov A, Abrams K, Mesenbrink P, et al. Renal safety of annual zoledronic acid infusions in osteoporotic postmenopausal women. Kidney Int. 2008;74:641-8.*
11. *Miller PD, Ragi-Eis S, Mautalen C, Ramirez F, Jonkanski I. Effects of intravenous ibandronate injection on renal function in women in postmenopausal osteoporosis at high risk for renal disease—the DIVINE study. Bone 2011;49:1317.*
12. *Health Science Authority website. 16 Aug 2010: Zoledronic acid (Aclasta®) and rare reports of renal impairment. http://www.hsa.gov.sg/content/hsa/en/Health_Products_Regulation/Safety_Information_and_Product_Recalls/Product_Safety_Alerts/2010/zoledronic_acid.html (Accessed 20 Sep 2017)*
13. *Bergner R, Henrich D, Hoffmann M, Schmidt-Gayk H, Lenz T, Upperkamp M. Treatment of reduced bone density with ibandronate in dialysis patients. J Nephrol 2008;21(4):510-6.*
14. *Wetmore JB, Benet LZ, Kleinstuck D, Frassetto L. Effects of short-term alendronate on bone mineral density in haemodialysis patients. Nephrology (Carlton) 2005;10(4):393-9.*
15. *Jamal SA, Ljunggren O, Stehman-Breen C, Cummings SR, McClung MR, Goemaere S, et al. Effects of denosumab on fracture and bone mineral density by level of kidney function. J Bone Miner Res 2011;26:1829-35.*
16. *Block GA, Bone HG, Fang L, Lee E, Padhi D. A single-dose study of denosumab in patients with various degrees of renal impairment. J Bone Miner Res 2012;27(7):1471-9.*
17. *Ishani A, Blackwell T, Jamal SA, Cummings SR, Ensrud KE; MORE Investigators. The effect of raloxifene treatment in postmenopausal women with CKD. J Am Soc Nephrol 2008;19:1430-8.*
18. *Weisinger JR, Heilberg IP, Hernández E, Carlini R, Bellorin-Font E. Selective estrogen receptor modulators in chronic renal failure. Kidney Int Suppl 2003;85;S62-5.*
19. *Palcu P, Dion N, Ste-Marie LG, Goltzman D, Radziunas I, Miller PD, et al. Teriparatide and bone turnover and formation in a hemodialysis patient with low-turnover bone disease: a case report. Am J Kidney Dis 2015;65:933.*



***MS SHIRLENE HO** is a pharmacist in the Department of Pharmacy, Tan Tock Seng Hospital.*



RADIOLOGY QUIZ

A 52-year-old Chinese male with no significant past medical history presented with non-specific back pain of two months' duration. There were no 'red flag' symptoms and he denied any fever or night sweats. There were no associated neurological signs. Plain lumbar spine radiographs on this current admission showed age-appropriate degenerative changes but was otherwise unremarkable. Significant laboratory results were haemoglobin 13.0 g/dL (reference range 13.0-17.0), white blood cell 9.6 x10^9/L (3.6-9.3), ESR 54 mm/hr (1-10), C-reactive protein 23.0 mg/L (0.0-5.0).

On examination, he had bilateral paraspinal tenderness over the lumbar spine region. The range of motion was slightly decreased. The gait was steady. Power, sensation and reflexes were normal. As he had prolonged symptoms which did not correlate with the radiographic findings, an MRI of the lumbar spine was arranged.

QUESTION 1

Below are selected images from the lumbar spine (figures 1 and 2). What do they show?

SAG T2W STIR **SAGT T1W** **SAG T1W with contrast**

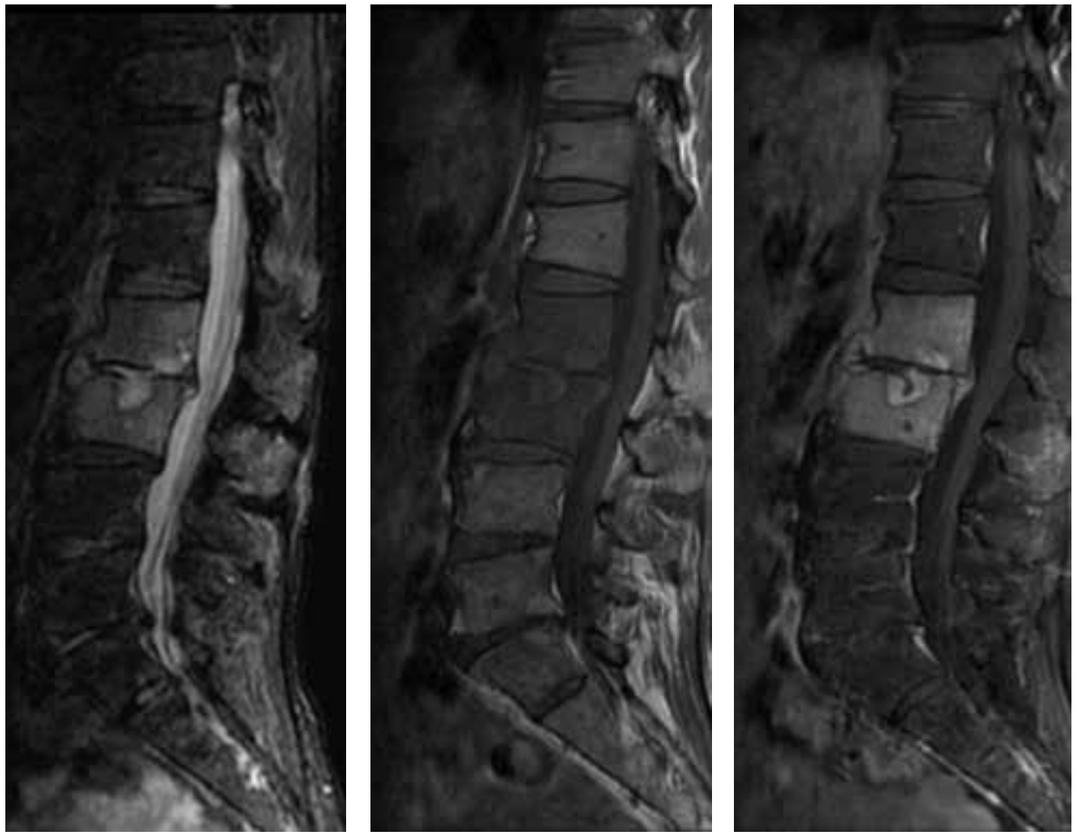


Figure 1. Images from the lumbar spine MRI study showing the sagittal STIR, sagittal T1W, sagittal T1W with contrast and Axial T1W with contrast sequences.

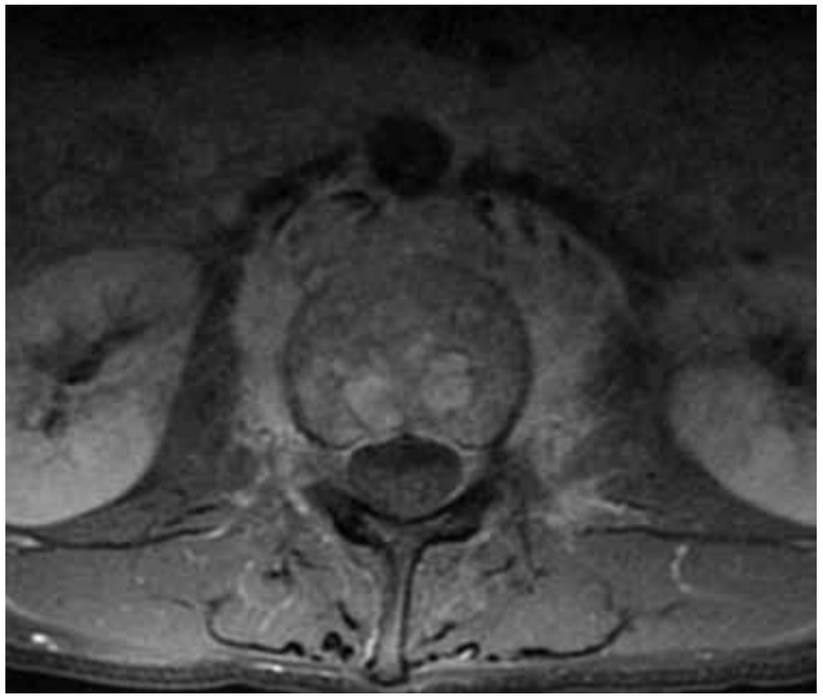


Figure 2. Image from the lumbar spine MRI showing Axial T1W with contrast at the L3 level.

QUESTION 2

What are the differential diagnoses in this patient?

ANSWER 1

The selected MRI images show homogeneous low T1W and bright T2W STIR signal involving the L2 and L3 vertebral bodies as well as the L2/3 intervertebral disc with reduced disc height and homogenous enhancement of the vertebral bodies. Schmorl's nodes are also seen at the inferior L2 and superior L3 end plates which can be physiological in nature (white arrow, figure 3).

On the post-contrast enhanced sequences there is abnormal enhancing soft tissue (white stars) around the vertebra with a small enhancing posterior epidural component (white arrow) (figure 4). No pathological fracture or rim-enhancing abscess is seen.

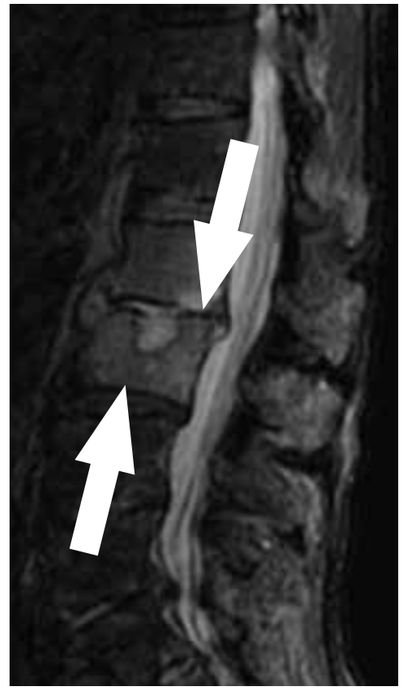


Figure 3. Sagittal image showing Schmorl's nodes.

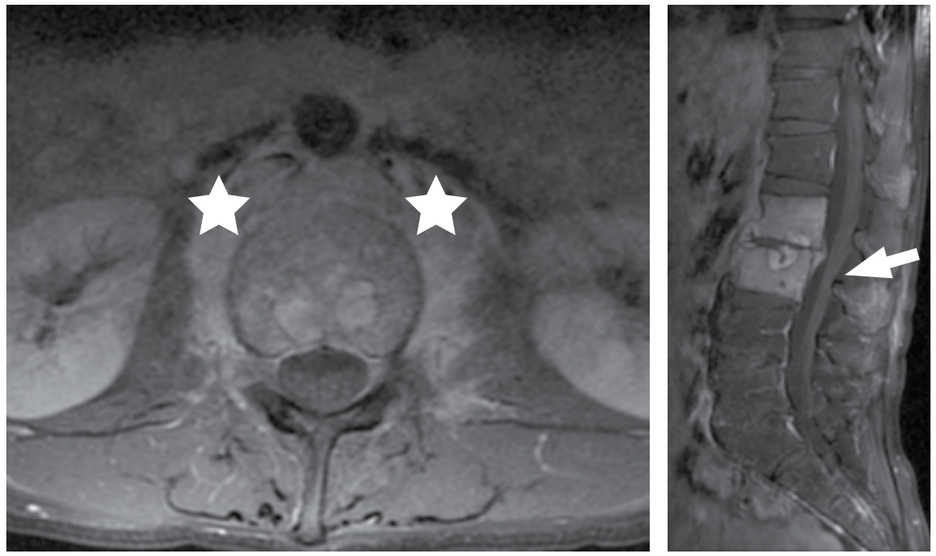


Figure 4. Post-contrast enhanced sequences showing abnormal enhancing soft tissue (white stars) around the vertebra with a small enhancing posterior epidural component (white arrow).

ANSWER 2

The top differential diagnosis is spondylodiscitis of infective or inflammatory cause in view of the homogenous involvement of two contiguous vertebral bodies as well as an abnormal signal within the intervening disc. This is supported by the soft tissue enhancement around the vertebra and the raised acute phase reactants ESR and CRP. Common culprit organisms include tuberculosis (Pott's disease), *Staphylococcus sp* or *Streptococcus sp*. A less likely differential is bony metastases in view of the abnormal marrow signal although one should see a more focal lesion within the vertebra with other lesions scattered across the rest of the spine.

Due to the diagnostic dilemma in this patient (absence of fever or underlying co-morbidities), he was referred to the Interventional Radiology team for a bone biopsy under CT guidance (figure 5). The biopsy culture returned *Staphylococcus caprae* which was sensitive to vancomycin. The patient was referred to the outpatient antibiotic therapy service for intravenous treatment.

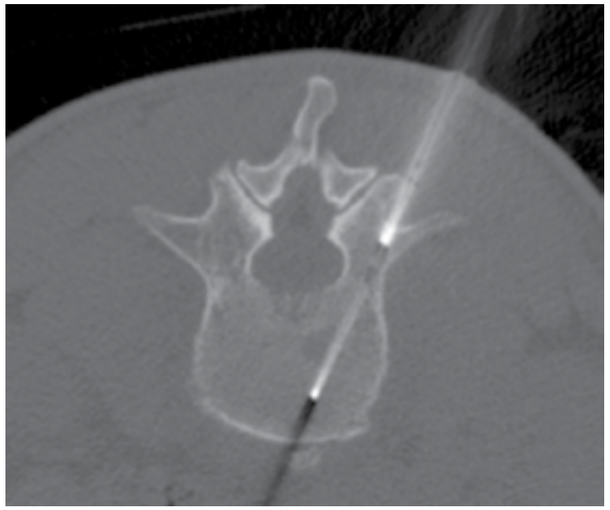


Figure 5. Bone biopsy under CT guidance.

Discussion

Spondylodiscitis is infection of the intervertebral disc and adjacent vertebrae. The typical presentation can be insidious although most patients present with fever (which may be low grade) and back pain. Some patients have other sources of bacteraemia as arising from endocarditis and intravenous drug use.

Some common risk factors include underlying known source of bacteraemia with involvement of the spine, previous spinal instrumentation or trauma, immunosuppression, long-term systemic administration of steroids and diabetes mellitus. Invariably, most patients would present with abnormal biochemical markers with elevated serum CRP and/or ESR.

Common organisms include *Staphylococcus aureus* (this is the commonest causative organism, found in 60% of cases), *Streptococcus viridans* (especially in intravenous drug users and immunocompromised individuals), gram-negative organisms (such as *Enterobacter spp* and *E. coli*), *Mycobacterium tuberculosis* and fungi (such as *Cryptococcus neoformans* and *Candida spp*).

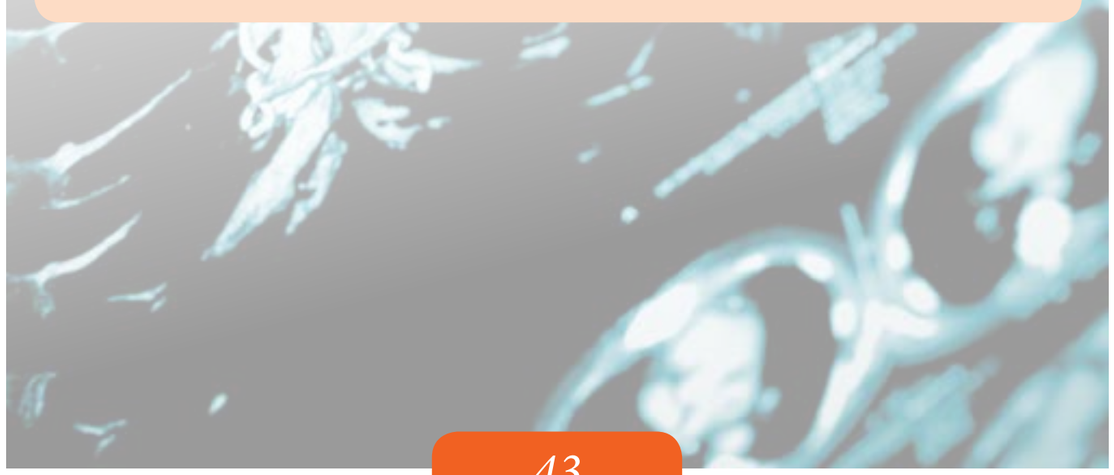
Spondylodiscitis can occur anywhere in the vertebral column but commonly involves the lumbar spine. Plain radiography is insensitive in the early changes of discitis/osteomyelitis, with normal appearances being maintained for up to 2-4 weeks. Thereafter disc space narrowing and irregularity or ill-definition of the vertebral endplates can be seen. In untreated cases, bony sclerosis may begin to appear in 10-12 weeks. MRI is the imaging modality of choice due to very high sensitivity and specificity. It is also useful in differentiating between pyogenic infection, tuberculous and fungal infections or neoplasm.

Treatment would vary on the severity and extent of involvement but the mainstay of treatment would be intravenous antibiotics and surgical/radiological drainage if there are any surrounding soft tissue abscesses or epidural involvement with neurological compromise.

FURTHER READING

1. *Dagirmanjian A, Schils J, Mchenry M et al. MR imaging of vertebral osteomyelitis revisited. AJR Am J Roentgenol. 1996;167 (6): 1539-43.*
2. *Dunbar JA, Sandoe JA, Rao AS et al. The MRI appearances of early vertebral osteomyelitis and discitis. Clin Radiol. 2010;65 (12): 974-81.*
3. *Falade OO, Antonarakis ES, Kaul DR et al. Clinical problem-solving. Beware of first impressions. N Engl J Med. 2008;359 (6): 628-34.*
4. *Ledermann HP, Schweitzer ME, Morrison WB et al. MR imaging findings in spinal infections: rules or myths? Radiology. 2003;228 (2): 506-14.*
5. *Ritchie DA. Commentary on the MRI appearances of early osteomyelitis and discitis. Clin Radiol. 2010;65 (12): 982-3.*
6. *Stäbler A, Reiser MF. Imaging of spinal infection. Radiol Clin North Am. 2001;39 (1): 115-35.*
7. *Oztekin O, Calli C, Adibelli Z et al. Brucellar spondylodiscitis: magnetic resonance imaging features with conventional sequences and diffusion-weighted imaging. Radiol Med. 2010;115 (5): 794-803.*

DR JUSTINE KWAN
is an associate consultant in the Department of Diagnostic Radiology,
Tan Tock Seng Hospital.



ECG QUIZ

A 50-year-old lady presented to the Emergency Department (ED) with a one-day history of episodic giddiness and loss of consciousness. This was associated with recurrent vomiting and diarrhoea for three days. She has a history of hypertension, dyslipidaemia and chronic alcohol use.

The resting 12-lead electrocardiogram (ECG) was performed in the ED (figure 1).

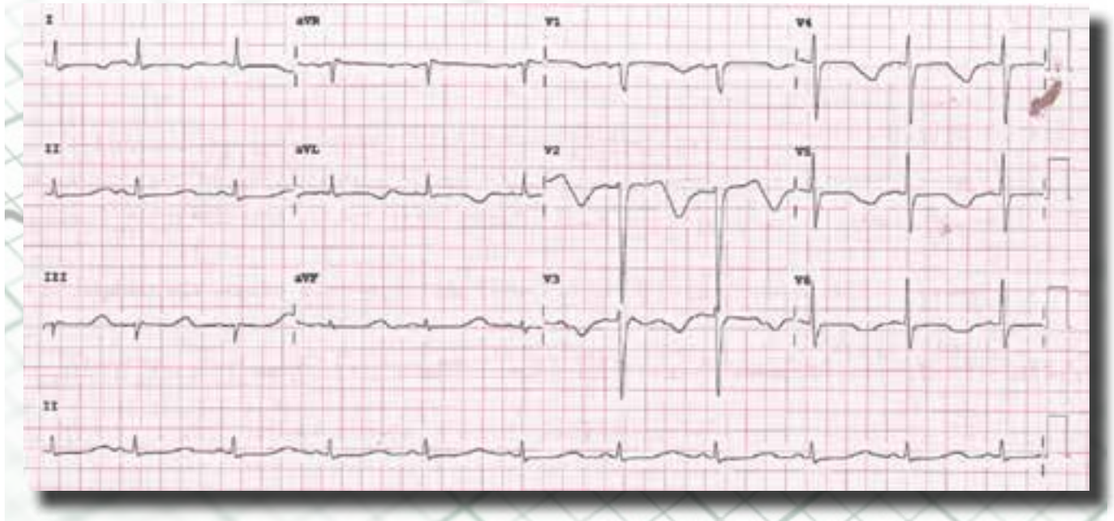


Figure 1. Resting 12-lead ECG performed at the Emergency Department on presentation.

QUESTIONS

1. Based on the ECG, what is the most likely reason for her loss of consciousness?
2. What further investigations should be performed?

ANSWERS

1. Arrhythmia resulting from prolonged QT interval.
2. Serum electrolytes especially potassium, calcium and magnesium levels.

Subsequent clinical course:
In view of the abnormal ECG, the patient was placed on continuous ECG monitoring. During the ED consult, the patient suddenly lost consciousness with no pulse. The ECG showed polymorphic ventricular tachycardia (figure 2) which was treated immediately with manual external defibrillation (figure 3). Blood tests revealed severe hypokalaemia and hypomagnesaemia (likely from vomiting) which were aggressively replaced intravenously.

There were no further arrhythmia episodes and the patient's QT interval normalised on the repeat ECG performed several days later on discharge.

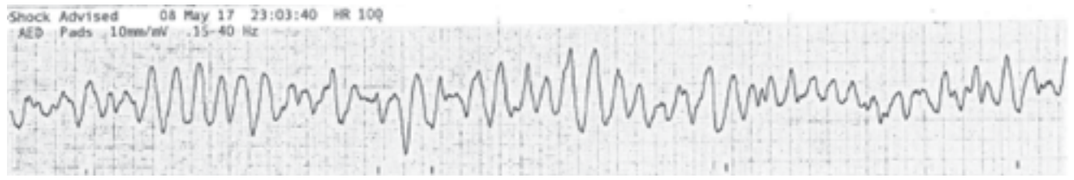


Figure 2. ECG rhythm strip taken when patient lost consciousness, demonstrating polymorphic ventricular tachycardia/torsades de pointes.

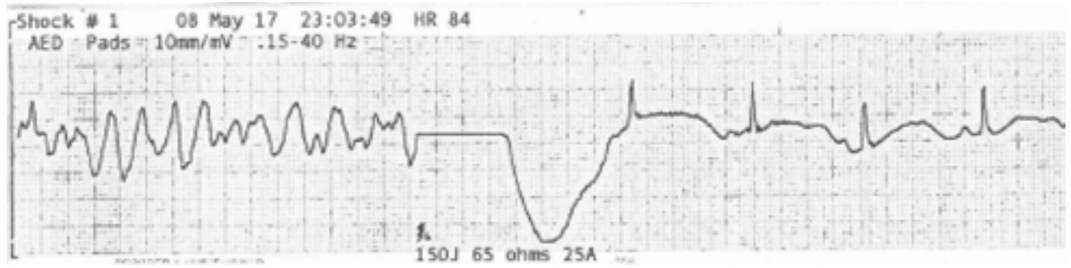


Figure 3. Reversion to sinus rhythm after 150 J external defibrillation.

Discussion

The QT interval represents the time taken for ventricular depolarisation and repolarisation and is measured from the beginning of the QRS complex to the end of the T wave. As the QT interval varies with heart rate, the corrected QT interval (QTc) is often calculated using the formula $QTc = QT/\sqrt{(R\text{-}R \text{ interval (seconds)}}$. The QT is considered prolonged when it exceeds 450 ms, although up to 470 ms is acceptable in women. As a general rule of thumb, the QT should not be more than half of the R-R interval on the ECG.

The QT interval may be prolonged due to primary causes (inherited long QT syndromes) although secondary causes are far more common. A drug history should be taken for offending medications (www.qtdrugs.org) such as antiarrhythmics, psychotropics and antimicrobials. Electrolyte disturbance such as hypokalaemia, hypocalcaemia and hypomagnesaemia should be excluded using blood tests.

A prolonged QT interval (especially when >500 ms) increases the risk of malignant arrhythmias such as polymorphic ventricular tachycardia. Also known as torsades de pointes, this life threatening arrhythmia demonstrates "twisting of peaks" of the QRS complexes around the isoelectric line on ECG. Urgent therapy with defibrillation, intravenous magnesium and correction of reversible causes is often effective in preventing further arrhythmic episodes.

REFERENCES
Adler Y, Charron P, Imazio M, et al. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases: The Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC). Eur Heart J. 2015; 36(42):2921-64.

DR YEW MIN SEN
is an associate consultant in the Department of Cardiology, Tan Tock Seng Hospital.