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Editorial

Bystander CPR: why all the fuss?

Simon Attard Montalto

In Europe, approximately one person suffers a cardiac arrest every 45 seconds, totalling 2-3,000 per day and 350,000 per annum.[1-2] Indeed, sudden cardiac arrest without resuscitation is the third most common cause of death in industrialised nations.[3] In the majority of cases, cardiac arrest is fatal and <10% of victims of 'out-of-hospital' arrest survive to discharge from hospital.[4] Furthermore, given that irreversible brain damage secondary to the cessation of cerebral blood flow is established within just 3-4 minutes, survival is often associated with significant neurological disability and an inferior quality of life compared with their pre-arrest state.[5-6] Cardiopulmonary resuscitation (CPR) associated with defibrillation, if delivered effectively and promptly within 1-2 minutes of cardiac arrest, may improve the chances of survival 3-4 fold or, rather more optimistically, to around 60%.[4-6] However, the 'time to intervention' is paramount and survival decreases by 10% for every minute delay in the initiation of CPR.[7-8] Conversely, studies from Denmark, amongst others, have shown that prompt initiation of effective bystander CPR will more than triple survival and save 200,000 victims in Europe and the US and, if extrapolated worldwide, save more than 300,000 lives per annum.[9]

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The vast majority of cardiac arrests occur in the community, away from a suitably equipped medical setting and are witnessed by bystanders in around 80% of cases.[10-11] In Malta in 2016-17, despite 71% of cardiac arrests being witnessed by laypersons, intervention only occurred in 39% of cases, including bystander defibrillation in 9% (data, MRC). It is not surprising, therefore, that the survival to discharge from hospital after out-of-hospital arrest in Malta was just 6% (data, MRC). The importance of good, bystander CPR cannot be underestimated. This requires laypersons to identify the signs of collapse, and be competent to initiate good CPR without delay and certainly before medical help arrives. In Malta, as elsewhere, the average time for an urgent ambulance to reach a victim varies but, even with optimal circumstances, this is likely to exceed 10 minutes[8] and is probably too late for most victims of cardiac arrest. So the timely intervention of laypersons is absolutely crucial if survival figures after an out-of-hospital cardiac arrest are to reach the European Resuscitation Council (ERC) goal of 60%. CPR and the use of an AED are relatively uncomplicated skills that can be mastered easily by non-medically trained laypersons.[12-13] This also applies to children whose retentive skills for the CPR algorithm may be better than adults, provided they are old enough to perform forceful and effective chest compressions.[14-15]

Malta is fortunate in that several bodies including the Malta Resuscitation Council (MRC), the Red Cross, St John Ambulance, Malta Heart Foundation, Order of St Lazarus and others, regularly provide courses in combined CPR-AED training. These, together with the MRC that runs ERC-certified courses, have set the standard of training required. To-date, the MRC alone has trained more than 2,000 medical personnel and 1,000 laypersons, and has helped train and equip the Health and Safety Unit within the Education Division who, so far, have trained around 300 schoolchildren. Whilst CPR-AED training is now mandatory for all medical students, General Practitioners and young hospital trainees are also

required to complete ILS and more advanced resuscitation courses. Ideally, all doctors, nurses and paramedics should complete basic training in CPR as a 'core skill'. Ultimately, the aim would be for CPR-AED skills to be included in the National School Curriculum for all 14 year olds (i.e. at an age when children not encumbered with major examinations but mature enough to appreciate the importance of CPR and strong enough to deliver this effectively). This goal has been championed by the European Resuscitation Council's aptly named 'Kids Save Lives'[15-16] and 'Restart a Heart' Campaigns launched in 2013,[17] and is supported by the World Health Organisation in 2015.[18] So far, five European countries including Belgium, Denmark, France, Italy and Portugal, have mandated the requirement to introduce CPR training onto the Education Curriculum by law, whilst others including Malta have recommended this initiative.[19] In practice, however, the introduction of CPR training in schools is still not widespread, even in those countries where this initiative is mandatory.[9,19] To-date, both Ministers for Health and Education in Malta have endorsed the ERC's request to promote the 'Kids Save Lives' Campaign and to lobby the World Health Organisation to place CPR training on their annual agenda. Linking CPR training with specific job applications, for example in the hospitality and tourism sector, managerial/supervisory posts in large institutions, factories, etc, and before the award of a valid driving or maritime licence would also boost the number of trained laypersons. The advent of the 'Good Samaritan' act that is currently under debate in Parliament will protect both victims and rescuers, and will further encourage bystanders to act without fear 'of retribution'.

However, training alone without the availability of AEDs is suboptimal, especially in the case of cardiac arrest in adults where fibrillation is present in approximately 25-33% of cases.[20] At present there are almost 600 AEDs spread around the island, but most are located in private institutions and are not available to the public. Moreover, some of these AEDs are not operative, usually because the battery has lost charge and/or expired. Although the Malta International Airport, Air Malta planes, Gozo ferries, most schools, banks, some hotels, factories and social clubs, amongst others, do have at least one AED, Malta needs many more in key and accessible locations to be truly 'covered'. The Victoria Council responsible for the Gozo Citadel has recently taken the lead in this regard and work is ongoing to install 8 AEDs with 24/7 public access in Valletta. A mobile phone AED locator app for Malta is also 'work in progress'. Malta should strive to install (and maintain) AEDs in most if not all key positions where significant numbers of individuals are likely to aggregate. As in other countries and major cities, the distinctive AED locating sign (a green square with a medical cross, heart and lightning bolt) should be widely distributed and clearly visible in numerous locations. Only this eventuality, combined with a sufficient body of trained bystanders who can initiate CPR and operate an AED, will significantly improve our survival figures for out-of-hospital cardiac arrest and justify all the fuss!

References

1. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al; American Heart Association Statistics Committee; Stroke Statistics Subcommittee . Executive summary: heart disease and stroke statistics—2016 update: a report from the American Heart Association. Circulation. 2016; 133: 447–454
2. Strategies to Improve Cardiac Arrest Survival. Available at: http://www.nap.edu/catalog/21723/strategies-to-improve-cardiac-arrest-survival-a-time-to-act.
3. Taniguchi D, Baernstein A, Nichol G. Cardiac arrest: a public health perspective. Emerg Med Clin North Am. 2012; 30: 1–12.
4. Böttiger BW. "A Time to Act"—Anaesthesiologists in resuscitation help save 200,000 lives per year worldwide: schoolchildren, lay resuscitation, telephone-CPR, IOM and more. Eur J Anaesthesiol. 2015; 32: 825–827.
5. Mongardon N, Dumas F, Ricome S, Grimaldi D, Hissem T, Pène F, Cariou A. Postcardiac arrest syndrome: from immediate resuscitation to long-term outcome. Ann Intensive Care 2011; 1:45. Published online 2011 Nov 3. doi: 10.1186/2110-5820-1-45
6. Böttiger BW, Grabner C, Bauer H, Bode C, Weber T, M otsch J, Martin E. Long term outcome after out-of-hospital cardiac arrest with physician staffed emergency medical services: the Utstein style applied to a midsized urban/suburban area. Heart. 1999; 82: 674–679.
7. Wissenberg M, Lippert FK, Folke F, Weeke P, Hansen C M, Christensen EF, et al. Association of national initiatives to improve cardiac arrest management with rates of bystander intervention and patient survival after out-of-hospital cardiac arrest. JAMA. 2013; 310: 1377–1384.

8. Neumar RW, Shuster M, Callaway CW, Gent LM, Atkin s DL, Bhanji F, et al. Part 1: executive summary: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2015; 132: S315–S367.
9. Malta Hansen C, Zinckernagel L, Kjær Ersbøll A, Tjørnhøj, Thomsen T, Wissenberg M, et al. Cardiopulmonary resuscitation training in schools following eight years of mandating legislation in Denmark: a nationwide survey. J Am Heart Assoc. 2017; 6:e004128. DOI: 10.1161/JAHA.116.004128.
10. Spaite DW, Hanlon T, Criss EA. Prehospital cardiac arrest: the impact of witnessed collapse and bystander CPR in a metropolitan EMS system with short response times. Ann Emerg Med. 1990; 19: 1264-9.
11. Hostler D, Thomas EG, Scott S, Emerson SS, Christenson J, Stiell IG, Rittenberger JC, et al. Increased survival after EMS witnessed cardiac arrest. Observations from the Resuscitation Outcomes Consortium (ROC) Epistry - Cardiac Arrest. Resuscitation. 2010; 81(7): 826–830. Published online 2010 Apr 18. doi: 10.1016/j.resuscitation.2010.02.005.
12. Perkins GD, Handley AJ, Koster RW, Castrén M, Smyth MA, Olasveengen T, et al. Adult basic life support and automated external defibrillation section Collaborators. European Resuscitation Council Guidelines for Resuscitation 2015: section 2. Adult basic life support and automated external defibrillation. Resuscitation. 2015; 95: 81–99.
13. Greif R, Lockey AS, Conaghan P, Lippert A, De Vries W, Monsieurs KG. Education and implementation of resuscitation section Collaborators. European Resuscitation Council Guidelines for Resuscitation 2015: section 10. Education and implementation of resuscitation. Resuscitation. 2015; 95: 288–301.
14. Böttiger BW, Bossaert LL, Castrén M, Cimpoesu D, Georgiou M, Greif R, et al; Board of European Resuscitation Council (ERC) . Kids Save Lives—ERC position statement on schoolchildren education in CPR: "Hands that help—Training children is training for life". Resuscitation. 2016; 105: A1–A3.
15. Böttiger BW, Van Aken H. Training children in cardiopulmonary resuscitation worldwide. Lancet.2015; 385: 2353.
16. Semeraro F, Wingen S, Schroeder DC, Ecker H, Scapigliati A, Ristagno G, Böttiger BW.KIDS SAVE LIVES implementation in Europe: a survey through the ERC Research NET. Resuscitation. 2016; 107:e7–e9.
17. Restart a Heart campaign: https://www.erc.edu/about/restart
18. Böttiger BW, Van Aken H. Kids save lives—Training school children in cardiopulmonary resuscitation worldwide is now endorsed by the World Health Organization (WHO). Resuscitation. 2015; 94: A5–A7.
19. Böttiger BW, Semeraro F, Wingen S. "Kids Save Lives": Educating Schoolchildren in Cardiopulmonary Resuscitation Is a Civic Duty That Needs Support for Implementation. J Am Heart Assoc. 2017; 6:e005738. https://doi.org/10.1161/JAHA.117.005738.
20. Keller SP, Halperin HR. Cardiac Arrest: the Changing Incidence of Ventricular Fibrillation. Curr Treat Options Cardiovasc Med. 2015; 17(7): 392-9.

The Journal Editor on the 10th Malta Medical School Conference

Dear Colleagues,

You are aware that you are all invited to the triennial 10th Malta Medical School Conference. This will be held 29 th November 2018 - 1 st December 2018 at the Westin Dragonara Hotel in St. Julians. The event is the largest local medical meeting and is perforce highly multidisciplinary, with the presentations of papers and posters relating to clinical work and research that are carried out locally and overseas. Furthermore, a number of eminent Malta Medical School graduates working abroad, as well as renowned foreign colleagues, will deliver plenary lectures. On behalf of the Conference Scientific and Organising Committees, and of the Journal, we wish you a pleasant yet educational time at the conference. If you are presenting work, do please bear in mind that if you do not write up your research work as a formal paper/s, and succeed in publishing, it is as if your work simply has not been done. Please, we exhort you, go forth, write a scientific paper, and publish!

Cover Picture:
'Waterfront'
Acrylic
By Rosita Farrugia

Rosita Farrugia was born on 11th July 1952. She worked in Cardiac Lab and X-ray Dept. as a nurse. She worked in Italy with the Department of Peadiatrics for 12 years in Florence and Verona.
She went for missionary work for 2 years in Kenya and 2 years in Nigeria and also to Cosovo where they took 4 containers to the Red Cross. She is also a member in the Malta Council in the Voluntary sector and she is also a member of the Fraternity of Charles de Faoucauld.

Original Article

Term Admissions to Neonatal Intensive Care Unit: a Maltese observational study

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Abstract

Objective: This study aimed to identify the number of term infants admitted to the Maltese Neonatal and Paediatric Intensive Care Unit (NPICU) between January and June 2016, as well as factors contributing to their admission.

Methods: All term infants (37+ weeks gestation) born between January-June 2016, transferred from Central Delivery Suite or Obstetric Wards to NPICU were identified. Patient registers, electronic case summaries, and the National Obstetric Information System (NOIS) database were used, with approval from the Data Protection Office, to collect data for a retrospective case control study.

Results: Of the term infants born in these 6 months, 5.2% (101) were admitted to NPICU resulting in 42.6% of all admissions. The mean gestational age was 39 weeks (95% CI 38.8, 39.3) and mean birth weight was 3.3kg (95% CI 3.2, 3.4). More than half had been born by elective and emergency Caesarean section (26% and 27% respectively). Commonest reason for admission was respiratory distress (37%). Others included non-bilious vomiting (20%), congenital abnormalities (13%), hyperbilirubinaemia (8%), and infection (4%). Statistically significant factors associated with admission were operative delivery, threatened miscarriage and maternal infection during pregnancy, maternal insulin dependent diabetes mellitus, and low Apgar scores.

Conclusion: The significant contributing factors should be targeted and further evaluation over a longer time-frame with an interdisciplinary team carried out in an effort to reduce rate of admissions and improve quality of care.

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Keywords

Infant, Newborn, Term Birth, Intensive Care, Neonatal, Malta, Case-Control Studies

Introduction

The Neonatal and Paediatric Intensive Care Unit at Mater Dei Hospital (NPICU) in Malta, provides highly specialised care to ill term or preterm newborns as well as children up to three years of age. It provides complex nutritional and respiratory support, cardiorespiratory monitoring, as well as more focused nursing care. Whilst admissions to neonatal intensive care are generally thought of in the context of prematurity or congenital abnormalities, international literature suggests that admission of term neonates (born at 37 weeks of gestation or more) to these units, though unexpected, is not a rare occurrence.[1-5] This level of care is costly and leads to separation of the infants from their mother and family in the important early moments of life. Such admissions

can therefore be considered as adverse perinatal outcomes and require additional investigation.[6]

The objective of our study was to determine the number of term infants admitted to NPICU within a specific time-frame, as well as identify factors contributing to their admission. This could guide strategies which aim to reduce admissions of term infants and their length of stay in NPICU. The end result would be an improved family experience, by decreasing the period of separation between the newborns and their family unit, and an overall reduction in the burden on our healthcare system.

Methods

All term neonates (born at 37 weeks of gestation or more) born between January 2016 and June 2016, who were transferred from either the Central Delivery Suite or the obstetric wards to the NPICU, were identified. Patient registers, electronic case summaries, and the National Obstetric Information System (NOIS) database were used in order to collect data for a retrospective case control study. This included maternal demographic data, comorbidities, social and obstetric history, mode of delivery and neonatal factors such as birth weight, gestational age and reason for admission. Term infants born between January 2016 and June 2016 that were not admitted to NPICU were taken as controls. Fisher's exact test, Chi-square test, and unpaired *t* test (with a *p*-value of <0.05 taken to represent significance) were used to determine statistically significant associations between the collected factors and admission to NPICU. Approval was obtained from the Data Protection Office.

Results

A total of 2110 births were recorded during the selected 6-month period. Of these, 1935 were term infants. 101 (5.2%) of these term births were admitted to NPICU, resulting in 42.6% of all admissions (*n*=237) and 55.2% of neonatal admissions (*n*=183).

Of the 101 term admissions, 60 (59.4%) were male and 41 (40.6%) were female. 20 (19.8%) were non-Maltese. The mean gestational age was 39 weeks (95% CI 38.815, 39.284) and mean birth weight was 3.3kg (95% CI 3.196, 3.403). Mean length of stay was 8.8 days (95% CI 7.603, 10.060).

Mean maternal age was 29.5 years (95% CI 28.488, 30.502). 8 mothers (7.9%) were Rhesus negative. 60 (59.4%) were primiparous, 35 (34.7%) were multiparous, and 6 (5.9%) had an unknown parity.

Labour onset was spontaneous in 44 mothers (43.6%), induced in 21 (20.8%), via Caesarean section in 30 (29.7%), and unrecorded in 6 mothers (5.9%). More than half of these term neonates had been born by elective and emergency Caesarean section (*n*=26, 25.7% and *n*=27, 26.7% respectively). The rest were born via normal vaginal delivery (*n*=41, 41.6%) and by ventouse-assisted vaginal delivery (*n*=7, 6.9%). 92 neonates (91.1%) were born in the cephalic presentation, 6 (5.9%) in the breech presentation, and in 3 (3.0%) presentation was unknown. 28 neonates (27.7%) were transferred from the Central Delivery Suite, while 19 (18.8%) were transferred from the obstetric wards. Source of transfer was unrecorded for the other 54 neonates (53.5%).

The various reasons for admission are shown as a percentage of the total term admissions in Figure 1. The 'Other' category comprised reasons such as neonatal abstinence syndrome, bradycardia, hypotonia, and hypoglycaemia.

Statistically significant factors associated with admission of term infants to NPICU are shown in Table 1. Table 2 shows the factors for which no significant association with admission to NPICU was found.

***Figure 1**: Reason for Admission to NPICU*

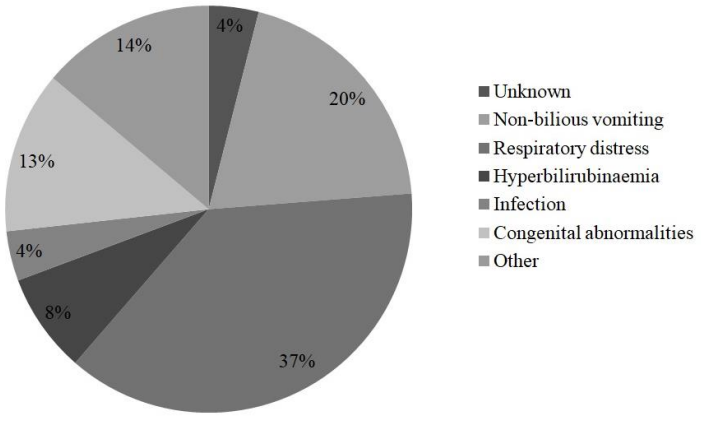

Table 1: *Statistically significant factors associated with NPICU admission*

Contributing factor	*p*-value	Odds Ratio	95% CI
Operative delivery	<0.001	2.865	1.904, 4.313
Threatened abortion	0.014	2.621	1.266, 5.424
Maternal infection	0.042	1.943	1.034, 3.652
Maternal IDDM*	0.035	9.242	1.672, 51.091
Low Apgar at 1 minute*	<0.001	7.100	4.137, 12.187
Low Apgar at 5 minutes*	<0.001	15.429	5.620, 42.359
*IDDM = insulin dependent diabetes mellitus; Low Apgar = score 0-6			

Table 2*: Non-statistically significant factors potentially contributing to admission*

Contributing factor	*p*-value	Odds Ratio	95% CI
Infant demographics			
Male	0.183	1.335	0.888, 2.007
Non-Maltese	1.000	1.007	0.609, 1.666
Gestational age	0.440	-	-
Birth weight	0.894	-	-
Maternal demographics			
Maternal age	0.274	-	-
Mother's education	0.404	-	-
Mother's height	0.831	-	-
Mother's weight at delivery	0.501	-	-
Mother's weight before pregnancy	0.204	-	-
Obstetric risk factors			
Maternal smoking	0.320	1.440	0.732, 2.835
Maternal alcohol use	0.102	18.330	1.137, 295.400
Maternal drug use	0.062	6.148	1.225, 30.864
Maternal cardiovascular disease	1.000	1.059	0.061, 18.481
Maternal NIDDM	1.000	6.021	0.244, 148.850
Artificial reproductive therapy	0.118	2.208	0.924, 5.275
Gestational age at first antenatal visit	0.728	-	-
Gestational hypertension	0.339	1.478	0.666, 3.280
Pre-eclampsia	0.313	3.047	0.363, 25.562
Gestational diabetes	0.254	1.624	0.636, 4.145
Suspected IUGR	0.767	0.630	0.152, 2.618
Twin delivery	0.489	1.373	0.417, 4.518
Antepartum haemorrhage	1.000	1.200	0.068, 21.178
Placenta praevia	1.000	1.069	0.141, 8.116
Placental abruption	0.102	18.330	1.137, 295.400
Threatened labour	1.000	0.781	0.046, 13.358

Discussion

In February 2017 NHS Improvement issued a resource pack and patient safety alert[6-7] to support safer care for full-term babies by reducing harm leading to their avoidable admission into neonatal units. This was in reaction to observed increasing rates of admission of term infants to intensive care (a 24% increase between 2011 and 2014), despite a downward trend in term live births (a decline of 3.6% between 2011 and 2014).[6] Unexpected admission of a term neonate to intensive care can be said to be a sign of preventable harm that may have occurred during the antenatal, intrapartum, or post-natal period. Admission to neonatal intensive care means separation of the infant from the mother which can lead to difficulties with breast feeding and bonding, as well as have a negative effect on maternal mental health.[8] It also increases the burden on a healthcare system[6] in terms of bed availability, economic cost, and staff to patient ratios. Keeping mother and baby together is therefore a case of getting it right from the start since it improves health outcomes for both in the short and long term.[6,9]

Using a 2-sample z-test, the local rate of term admissions to intensive care of 42.6% for the 6 month period studied was found to be lower than the rates for England in 2011, 2012, and 2013 (56.6%, 58.3%, and 59.8% respectively, $p<0.001$).[10] However, since the Maltese unit is both a neonatal and paediatric intensive care unit, catering for children up to three years of age, this rate of 42.6%, though reflecting the local burden on the unit, cannot be used to compare with rates in the UK which take into account only admissions to a neonatal unit. Indeed the rate of 55.2% which represents the term admissions as a percentage of only neonatal admissions is comparable to the rates in England between 2011 and 2013 ($p=0.705$, $p=0.397$, $p=0.203$ respectively). It is also important to point out that in Malta, when compared to the UK, access to a neonatal unit might relatively be easier, there being only one general hospital and one unit in the same hospital catering for the whole population.

The commonest reason for admission in the studied 6 month period was respiratory distress, accounting for 37.6% of admissions. Respiratory distress was also the commonest reason for admission of term infants in the UK with 25% of admissions having this listed as their main reason for admission.[6] A quarter of these respiratory distress admissions in both Malta and the UK had been delivered by elective Caesarean section.[6] The risk of respiratory morbidity is known to be increased in babies born by Caesarean section before labour, but this risk is decreased if elective Caesarean section is performed after 39 weeks.[11] Thus NICE guidance recommends that elective Caesarean section is not performed prior to 39 weeks.[12]

Admission due to non-bilious vomiting was also another important reason for admission locally, at 19.8% of all term admissions. Non-bilious vomiting may indicate a primarily feeding problem, ranging from normal variation to overfeeding, to gastro-oesophageal reflux disease. Further evaluation of such admissions to determine what management was required would be necessary to properly classify the reason for admission.

The 12.9% admitted due to congenital anomalies can be said to be expected admissions to intensive care. There was no data regarding the severity and type of congenital anomaly, and whether this had been diagnosed antenatally and if admission had been planned beforehand.

Admissions for hyperbilirubinaemia accounted for 7.9% of term admission to the intensive care unit. Other term neonates with hyperbilirubinaemia would have been admitted to the general paediatric wards if less aggressive management was deemed necessary. This is an example of where a transitional care model can be applied. Admission for the indicated medical care may be necessary and unavoidable. However certain services may be provided outside the neonatal unit in a transitional care model where the mother is resident with her child and plays a role in providing care.[6] Transitional care, apart from providing an alternative setting for admission, may also lead to earlier discharge from the intensive care unit, acting as a bridge prior to definite discharge home.

4% of admissions were reported to be due to infection. However, other commoner reasons for admission, such as respiratory distress or non-bilious vomiting, could have very well been the first sign of sepsis, and thus this could be an under-estimation. Classifying admissions according to diagnosis on discharge may be more indicative of the true reason why the neonate needed admission to the unit. On the other hand using the recorded reason on admission demonstrates which presenting

symptoms are causing term neonates to be admitted in the first place.

Hypoglycaemia was the third commonest cause for admission in the UK[6], but in Malta only 2 out of the 101 term admissions had hypoglycaemia recorded as their principal reason for admission. Hypoglycaemia could have been present but not regarded as the main reason for admission, thus leading to its under-estimation.

In the case-control part of our study various possible contributing factors were assessed to determine whether there was a significant association with admission to NPICU. Operative delivery, including emergency and elective Caesarean section and instrumental delivery, was found to be significantly associated with admission to the neonatal unit. This could be interpreted as babies who are born by Caesarean section or by an assisted delivery are more likely to be admitted to intensive care. However whether this is due to the mode of delivery itself or the underlying reason for the need of an operative delivery (such as foetal distress leading to emergency Caesarean section) is not clear.

Threatened miscarriage during pregnancy, presenting mostly as vaginal bleeding during pregnancy, was also found to be significantly associated with admission to NPICU. This has also been demonstrated in studies elsewhere.[13-14]

The category maternal infection during pregnancy in our study included hepatitis C positive mothers, vaginal infections, urinary tract infections, and vulval warts. However in our study, the 2 mothers that were hepatitis C positive were ex-intravenous drug users on methadone and their babies were admitted to NPICU due to neonatal abstinence syndrome rather than due to signs of sepsis.

Type 1 diabetes in mothers was also found to be associated with admission to neonatal intensive care. Infants of diabetic mothers can be macrosomic or small for gestational age, are at an increased risk of neonatal hypoglycaemia, polycythaemia, respiratory distress syndrome, and congenital anomalies. Interestingly however, no significance was found for association between non-insulin dependent diabetes or gestational diabetes and admission to NPICU. Since pregnancy is itself diabetogenic, it may be an additional challenge for glucose control in insulin dependent diabetics as insulin requirements will change.

Low Apgar scores indicate inappropriate adaption to extra-uterine life, and thus admission to NPICU may be said to be expected in such cases. A low Apgar score may therefore alert the clinician to a possibly at risk neonate.

With regards to the other possible contributing factors assessed, significance may have not been achieved due to the small numbers used in the study. No cases of eclampsia in either the cases or controls were reported and this could be due to both the study's small sample size as well as its short time-frame. Other limitations include incomplete medical record-keeping in the patient registers from which the raw data was collected, and confounding variables which might not have been taken into account. Such limitations lead to the recall bias commonly attributed to retrospective studies as well as the inability to predict whether admission of term infants to NPICU was in fact preceded by exposure to a risk factor. The first step in overcoming these limitations is the introduction of an electronic database in order to ensure standardisation of accurate and timely data compilation.

The above results have been communicated to the relevant stakeholders at various departmental meetings. Increasing staff awareness and providing tools for training and education is essential to bring about quality improvement. Health Education England (Wessex) for example have commissioned a multi-disciplinary interactive eLearning resource and the British Association of Perinatal Medicine (BAPM) has proposed the Newborn Early Warning Trigger and Track (NEWTT) charts as an early warning score system for neonates.[15-16] An effort towards improving all aspects of antenatal, intrapartum, and postnatal care is necessary and this would require an inter-disciplinary approach with good communication between the different healthcare professionals taking care of both mother and baby.

In order to be able to put all this into practice a targeted working group, made up of a multidisciplinary team involving obstetricians, midwives, neonatal nurses, neonatologists, and paediatricians, is being suggested. Such a working group could review admissions case by case and thus determine what care was provided, what the diagnosis at discharge was, whether admission was justified in retrospect, and whether an alternative setting of admission could have been possible, amongst other aspects. Such an evaluation over a

longer time frame may guide the setting up of specific local guidelines (such as guidelines on criteria for admission to NPICU) and the implementation of practical strategies to improve neonatal care.

This study has identified a considerable number of term admissions to NPICU during the stipulated time period, highlighting respiratory distress as the most common cause of admission. Several factors have been described which have been found to contribute towards these admissions, including operative delivery, threatened miscarriage, maternal infection, and maternal IDDM. It is advised that a working group is set up which can eventually use this information to suggest practical strategies which will minimise term admissions to NPICU. This will result in keeping mother and baby together, proven to improve health outcomes in the short and long term for both, as well as alleviate some of the burden on our healthcare system.

Acknowledgments

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References

1. Granger C, Okpapi A, Peters C, Campbell M. PA.48 Expected and Unexpected Term Admissions to Neonatal Intensive Care (NICU). Arch Dis Child Fetal Neonatal Ed 2014;99:A32.
2. Harrison W, Goodman D. Epidemiologic Trends in Neonatal Intensive Care, 2007-2012. JAMA Pediatr 2015;169:855-62.
3. Ram Mohan A, Chawda N, Misra I. Term Admissions to the Neonatal Unit; Are They Avoidable? Arch Dis Child Fetal Neonatal Ed 2013;98:A17-A18.
4. Thankappen RA, Chetcuti Ganado C. Unexpected term admissions to the neonatal unit: Can the burden be reduced ? Arch Dis Child Fetal Neonatal Ed 2014;99:A56.
5. Tracy SK, Tracy MB, Sullivan E. Admission of term infants to neonatal intensive care: a population-based study. Birth 2007;34:301-7.
6. NHS Improvement. Reducing harm leading to avoidable admission of full-term babies to neonatal units. London: NHS Improvement, 2017.
7. NHS Improvement. Patient Safety Alert: Resources to support safer care for full-term babies. London: NHS Improvement, 2017.
8. Crenshaw JT. Healthy Birth Practice #6: Keep Mother and Baby Together— It's Best for Mother, Baby, and Breastfeeding. J Perinat Educ 2014;23:211–7.
9. Crenshaw JT. Care Practice #6: No Separation of Mother and Baby, With Unlimited Opportunities for Breastfeeding. J Perinat Educ 2007;16:39–43.
10. Attrell V. Insight into a Network approach to ATAIN: action plan to reduce term admissions. [Presentation] How to Reduce your Neonatal Term Admissions. 17th May 2017.
11. Morrison JJ, Rennie JM, Milton PJ. Neonatal respiratory morbidity and mode of delivery at term: influence of timing of elective caesarean section. Br J Obstet Gynaecol 1995;102:101-6.
12. National Institute for Health and Care Excellence. Caesarean section (NICE guidelines CG132). London: National Institute for Health and Care Excellence, 2011.
13. Nagy S, Bush M, Stone J, Lapinksi RH, Gardó S. Clinical significance of subchorionic and retroplacental hematomas detected in the first trimester of pregnancy. Obstet Gynecol 2003;102:94-100.
14. Petriglia G, Palaia I, Musella A, Marchetti C, Antonilli M, Brunelli R, et al. Threatened abortion and late-pregnancy complications: a case-control study and review of literature. Minerva Ginecol 2015;67:491-7.
15. NHS Health Education England. Reducing Avoidable Term Admissions. Available from: https://hee.nhs.uk/hee-your-area/wessex/our-work/research-innovation/elearning/mobile-learning/reducing-avoidable-term-admissions [Accessed 8th October 2017].
16. British Association of Perinatal Medicine. Newborn Early Warning Trigger & Track (NEWTT) - a Framework for Practice. Available from: https://www.bapm.org/resources/newborn-early-warning-trigger-track-newtt-framework-practice [Accessed 8th October 2017].

Plethysmography and its relationship with biochemical parameters in the Maltese population

Theresia Dalli, Sara Xuereb, Peter Fsadni, Stephen Montefort

Abstract

Plethysmography is an ever increasing test being performed at Mater Dei Hospital. The aim of the study was to obtain descriptive data regarding plethysmography in the Maltese population as well as to investigate the association of these lung function tests to various biochemical parameters.

282 patients who had plethysmography between June 2015 and March 2016 at Mater Dei Hospital were enrolled in the study. The indications for referral, demographic data, lung function parameters, white cell count (WCC), urea, potassium and fasting blood glucose were noted. The mean BMI of the population cohort was 29.06 (SD +/- 6.16). BMI was found to be negatively correlated to serum potassium levels (r=-0.14) and residual volume (r=-0.2). Diffuse lung capcicity of Oxygen (DLCO), total lung capacity and forced expiratory flow in one second were negatively correlated to the WCC (r=-0.2, r=-0.17 and r=-0.12 respectively) in the population. The current study confirms a significant association between lung function testing, diabetes, BMI and total serum white cell count after correcting for confounding factors. This highlights the need for clinicians to be more aware of the possibility of underlying lung disease in these patients. A good clinical evaluation using history and examination of such patients is essential so as to identify which patients should be referred for lung function testing. Such early referrals could potentially avoid progression of undiagnosed lung disease thus reducing the burden on the health care service with particular emphasis on acute hospital admissions and respiratory outpatient clinics.

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Keywords

plethysmography, leukocytes, obesity, diabetes

Introduction

Whole body plethysmography is the test of choice whenever information regards absolute lung volumes is required in addition to the spirometry results. Plethysmography should be performed on patients with suspected restrictive lung diseases where the measured lung volumes can help to differentiate between an obstructive and a restrictive pattern. Plethysmography is also useful

in the evaluation of obstructive lung diseases such as cystic fibrosis and bullous emphysema as well as to assess the resistance to airflow. Moreover, it can be used during the course of the disease where it aids in assessing the response to treatment.[1]

Due to the challenges associated with performing and interpreting plethysmographies and the ever increasing amount of referrals for plethysmography at Mater Dei Hospital this study primarily aims to obtain descriptive statistics associated with plethysmography for the first time in Malta including appropriateness of referral. The secondary aim of the study was to investigate the association between lung function testing and various biochemical parameters thus helping clinicians during the overall evaluation of patients.

Materials and Method:

Patients

A total of 282 patients who had a plethysmography at the Mater Dei Pulmonary Function laboratory were included in this retrospective study. All patients who had plethysmography between June 2015 and March 2016 were included in the study, after permission to collect patient data was obtained from the hospital and data protection. Data collection included indications for referral, demographic data including age, gender, height and weight, total lung capacity (TLC), residual volume (RV), diffusion lung capacity for carbon monoxide (DLCO), forced expiratory volume in the 1st second (FEV_1), forced vital capacity (FVC) and the FEV_1 and FVC ratio.

Blood investigations including urea and creatinine, potassium, sodium, calcium, phosphate, magnesium, haemoglobin, white cell count, platelets, as well as fasting blood glucose and glycated haemoglobin taken within 2 months from the plethysmography study date were reviewed and documented for each patient. Data from the plethysmography test of patients who did not have any blood results were still collected for the purposes of studying the demographics of patients referred for plethysmogtaphy yet were then excluded in studying the associations of lung volumes to biochemical parameters. Previous chest X rays, Thoracic CT Scans and High resolution CT scans were reviewed in order to confirm underlying diagnosis.

Statistic

Patients were then subdivided according to the indication for which they were referred for plethysmography and the average age, weight, height and BMI for the male and female participants of each population were worked out together with standard deviation of the respective parameters. Weight, height and BMI are mandatory parameters for performing lung function testing and therefore all lung function tests reviewed had these patient parameters included.

The mean values were used for all parameters included in the study since normality testing showed a normal distribution of data. The Pearson correlation was performed to investigate (i) the linear correlation of age, height, weight and BMI with renal profile, electrolytes, CBC and plethysmography parameters and (ii) the linear correlation of DLCO, TLC, RV, FEV_1 and FVC with renal profile, electrolytes, CBC and plethysmography parameters. Double sided P-values were worked out.

Multiple regression analysis was carried out to investigate any interdependencies between the variables studied and to further evaluate the association between DLCO and weight, height, BMI, urea, creatinine, potassium, sodium, haemoglobin, platelets and WCC.

Analysis was performed using EXCEL13 and p-values of less than 0.05 were considered to be statistically significant.

Results

Demographic information of the patient cohort are as presented in Table 1.

Demographic data

A total of 153 males and 129 females participated in this study. A total of 43 patients were referred in view of diagnosis other than chronic obstructive pulmonary disease (COPD) or fibrosis (shown in Table 2 and Table 3) and these included asthma, bronchiectasis, pleural plaques, sarcoidosis, systemic sclerosis or neuromuscular disorders. In 54 of patients, no indication was documented on the referral ticket for plethysmography.

***Table 1**: Demographics of the cohort population: Means, standard deviation and 95% CI for the demographic, biochemical and lung function parameters*

Parameter	Mean	Standard Deviation	95% Confidence Interval (Mean)
Age	66	12.45	1.47
Weight	75.77	18.83	2.22
Height	161.13	9.65	1.14
BMI	29.06	6.16	0.72
Urea	6.96	4.97	0.59
Creatinine	87.49	43.35	5.14
Potassium	4.78	0.03	0.07
Sodium	141.03	4.12	0.49
Phosphate	1.11	0.23	0.04
Magnesium	0.83	0.13	0.06
Fasting Blood Glucose	6.08	1.87	0.26
HbA1c	45.9%	12.12	1.94
White cell count (WCC)	8.66	2.96	0.35
Haemoglobin	13.81	1.57	0.18
Platelets	268.24	104.97	12.46
Total Lung capacity (TLC)	103.9%	40.35	4.82
Residual volume (RV)	133.6%	98.50	11.80
Forced Expiratory Volume in 1s (FEV_1)	72.3%	49.47	6.07
Forced vital capacity (FVC)	67.9%	29.07	3.49
FEV_1/FVC	75.4%	17.28	2.12
Diffuse lung capacity (DLCO)	70.7%	32.33	4.11

***Table 2**: **Indication for referral for body plethysmography**:*
The greatest indication was in patients with lung fibrosis. Gender distribution is also shown. (COPD – chronic obstructive pulmonary disease)

Disease	Total number of patient referred (%)	Male (%)	Female (%)
Fibrosis	42.6%	49.2%	50.8%
COPD	18.4%	86.5%	13.5%
Hypersensitivity pneumonitis	4.6%	30.7%	69.2%
Other diagnosis incl. asthma, bronchiectasis, pleural plaques	15.3%		
No diagnosis found	19.1%		

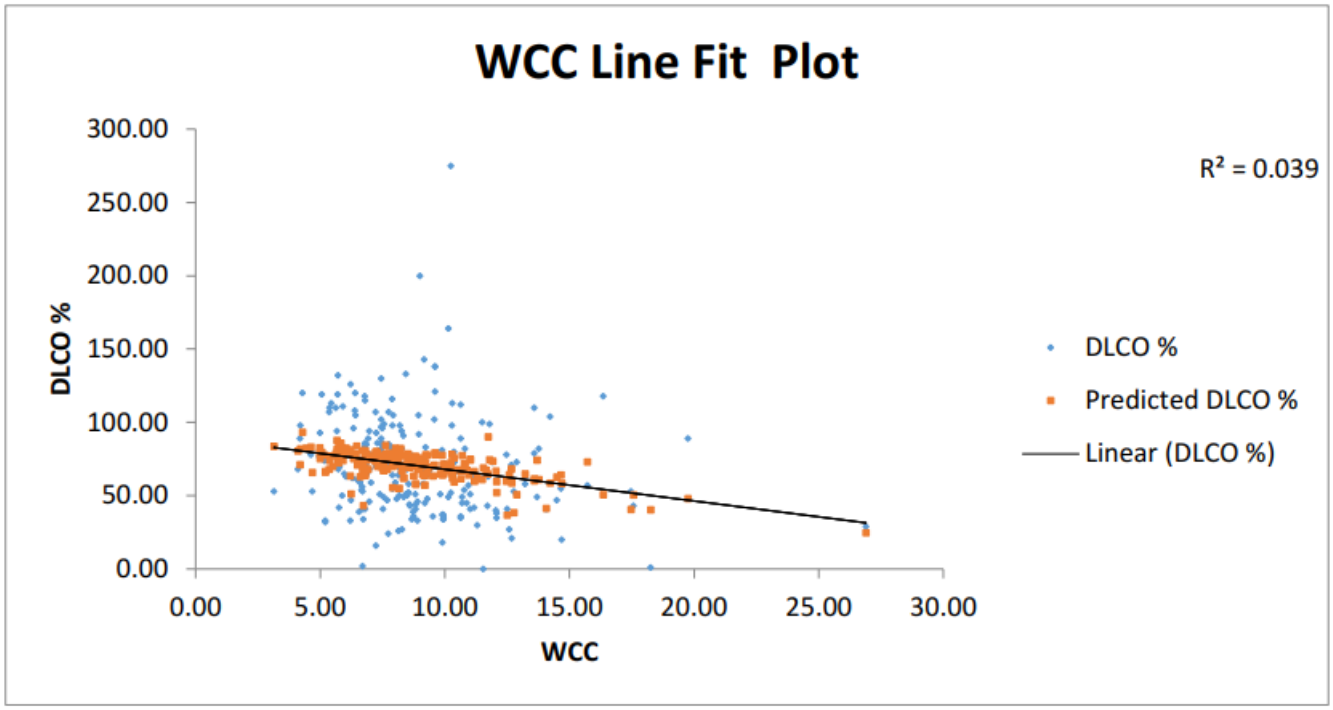
Table 3: Age, BMI and DLCO in the commonest presenting pathologies
Obesity has been noted across all the different groups as shown above.

	Mean Age		Mean BMI		Mean DLCO %	
Disease	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**
COPD	70.16	72.14	26.93	26.23	74	47
Fibrosis	68.23	67.93	29.42	28.64	64	62
Hypersensitivity pneumonitis	52.50	65.89	34.49	35.79	54	69

Table 4: Pearson Correlate between the variables studied
A statistically significant negative correlation was noted between the HbA1c and RV and FVC. There is also a negative correlation between FVC and urea. A clinically significant positive correlation between FVC and sodium was also noted.
(RV: residual volume, FVC: forced vital capacity, HbA1c (glycated haemoglobin)

Parameters	**R value**	**P value**
RV to Hba1c	-0.27	0.00077
FVC to Urea	-0.13	0.02
FVC to Sodium	0.13	0.04
FVC to Hba1c	-0.166	0.04

Figure 1: Multiple regression analysis showing the relationship of white cell count (WCC) and diffuse lung capacity of CO (DLCO)*: A statistically significant negative correlation was found showing that with impaired lung function patients are more likely to have raised WCC.*



The mean BMI of the population cohort studied was 29.06 (SD +/- 6.15). BMI was negatively correlated with serum potassium levels (r=-0.14, p=0.02) and positively correlated with calcium levels (r=0.21, p=0.02) after correcting for any confounding factors. Both TLC (r=-0.19, p=0.002) and RV (r=-0.2, p=0.001) were negatively correlated to BMI.

Plethysmography

The total mean white cell count of the studied population, was negatively correlated with the mean DLCO levels (r=-0.2 and p=0.002).

A similar association was also noted between the TLC and WCC (r=-0.17, p=0.006) and between FEV_1 and WCC (r=-0.12, p=0.05). Other associations between different parameters were also noted as documented in Table 4. No significant association was noted between DLCO and HbA1c (r=-0.06, p=0.52) or haemoglobin (r=0.06, p=0.32).

Multiple Regression Analysis

The association found between the DLCO and the WCC was confirmed when controlling for other factors including the weight, height, BMI, urea, creatinine, potassium, sodium, haemoglobin and platelets as shown in Figure 1. An R^2 value of 0.84 and a p value of 0.0004.

Discussion

In this first retrospective study targeting patients referred to Mater Dei Hospital for plethysmography, a total of 282 patients with respiratory disease, were investigated.

The study is the first large cohort, population based study relating the plethysmography results to the metabolic profile. One of the benefits of Malta being a small island, with one general hospital, is that all patients requiring plethysmography were referred to the same medical center. Moreover, the service is not provided in private hospitals and thus all patients requiring the test are referred to Mater Dei. This provided both lab and operator standardization hence, eliminating inter-operational and calibration errors.

All the patients referred for this investigation in the current study were suffering from chronic respiratory diseases such as pulmonary fibrosis, chronic obstructive pulmonary disease and asthma. These results highlight the need to better understand the indications of when a plethysmography study is needed during the clinical work up of patients since nearly 20% of referred patients were suffering from obstructive airway diseases only. This highlights the importance of not using this type of investigation in the management of such patients unless a specific indication such as review of diagnosis or lung transplant work up is being considered. The authors suggest the inclusion of a checklist contain the main indications for plethysmography on the current lung function test referral form. One limitation of this study is that no data regarding justification of referral of such patients for plethysmography was available since patients' clinical files were not accessed.

In Malta, like in many westernized countries, obesity is an increasing problem with an estimated 69.75% of the Maltese population being overweight or obese.[2] Obesity affects lung volumes with a negative correlation observed between increasing BMI and expiratory reserve volume (ERV) and functional residual capacity (FRC).[3] FRC in the obese individual is also linked to airway resistance and airway conductance. Airway resistance increases with an increasing BMI and this might lead to obesity-related problems with breathing. The total lung capacity (TLC), residual volume (RV) and vital capacity (VC) decrease proportionately with an increase in weight while an increase in DLCO is associated with increasing BMI.[3]

The current study demonstrates that the TLC, FEV_1 and DLCO was found to have a significant negative correlation with the total the peripheral white cell count (p=0.002). Multiple studies have also shown that peripheral leucocyte numbers are significantly higher among smokers versus non-/former smokers[4-11] contrary to what other evidence that suggests that the negative association between serum leucocyte count and FEV_1 is independent of smoking status.[4,11-14] Studies have shown that serum leucocyte count is also significantly inversely correlated with FVC.[4, 12] This trend was also noted in our study, however the results were not found to be statistically significant. One potential limitation of the current study is that the differential white cell count was not investigated since serum neutrophil counts have been associated with a decrease in DLCO.[15]

Results from two longitudinal studies over a period of years affirm that raised serum leucocytes are not only related to poor initial pulmonary function, but are moreover a predictor of follow up

decline in lung function[12-13] and a significant predictor for respiratory symptoms both among smokers and non-smokers. [16] A low FEV_1 and a raised WCC have both been shown to be independent predictors of increased all cause mortality rate. [11] Our findings are thus in keeping with those of previous studies suggesting that the serum leucocyte count is an important independent determinant of lung function, irrespective of smoking status.[4, 15]

Since the prevalence of diabetes in the Maltese population is 10.39% [1] the current study has focused on the association between lung function tests and diabetes. Results showed that worsening glucose control, as measured by glycated haemoglobin level, was significantly associated with a low RV and low FVC. Two studies reported a similar relationship between Hba1c and FVC [17] while multiple studies have shown that pulmonary function is indeed reduced in patients with both type 1 and type 2 diabetes mellitus.[17-20] Patients with a decreased RV have restrictive lung disease for which long-term steroids are prescribed. Steroids are known to have a profound effect on glucose metabolism and hence, it is essential that patients receiving therapy have their Hba1c monitored regularly.

There is however conflicting evidence regarding the relationship between Hba1c and lung function tests. In fact, some evidence suggests that duration of diabetes is a more significant factor for poor respiratory function.[18,20-22] Conversely, research also shows that lung function is inversely related to the risk of future diabetes.[23–27] Of note is that diabetes is a significant influencer for low DLCO.[19-22] This trend has been observed in our study but was not found to be statistically significant.

The lack of data regarding the smoking status of patients participating in the study as well as the presence of multiple comorbidities that might be affecting the results are potential limitations of the study.

The current study confirms a significant association between lung function testing, diabetes, BMI and total serum white cell count after correcting for confounding factors. This is of particular relevance in the Maltese population which has a high prevalence of obesity and diabetes when compared to other European countries. Since most of the patients recruited in the study were of Maltese background (as stipulated from their ID numbers), the authors propose that there might be an underlying genetic, environmental and geographical predisposition to pulmonary pathology in this cohort of patients. This highlights the need for clinicians to be more aware of the possibility of underlying lung disease in these patients. A good clinical evaluation using history and examination of such patients is essential so as to identify which patients should be referred for lung function testing. Such early referrals could potentially avoid progression of undiagnosed lung disease thus reducing the burden on the health care service with particular emphasis on acute hospital admissions and respiratory outpatient clinics.

References

1. Townsend Rocchiccioli J, O'Donoghue CR, Buttigieg S. Diabetes in Malta: Current findings and future trends. *Malta Medical Journal*. 2005; 17(1): 16-19
2. Cuschieri S, Vassallo J, Calleja N, Camilleri R, Borg A, Bonnici G, et al. Prevalence of obesity in Malta. Obesity science and practice. 2016; 2(4): 466-470
3. Jones R, Nzekwu MM. The effects of body mass index of lung volumes. Chest. 2006; Sep 130(3): 827-33
4. Chan-Yeung M, Dy Buncio A. Leukocyte count, smoking, and lung function. Am J Med 1984; 76: 31-7.
5. Corre F, Lellouch J, Schwartz D. Smoking and leucocyte-counts: Results of an epidemiological survery. Lancet 1971; 298: 632-4.
6. Friedman GD, Siegelaub AB, Seltzer CC, Feldman R, Collen MF. Smoking habits and the leukocyte count. Arch Environ Health 1973; 26: 137-43.
7. Chan-Yeung M, Ferreira P, Frohlich J, Schulzer M, Tan F. The effects of age, smoking and alcohol on routine laboratory tests. Am J Clin Pathol 1981; 75: 320-6.
8. Petitti DB, Kipp H. The leukocyte count: Associations with intensity of smoking and persistence of effect after quitting. Am J Epidemiol 1986; 123: 89-95.
9. Jensen EJ, Pedersen B, Frederiksen R, Dahl R. Prospective study on the effect of smoking and nicotine substitution on leucocyte blood counts and relation between blood leucocytes and lung function. Thorax 1998; 53: 784-9.
10. Noble RC, Penny BB. Comparison of leukocyte count and function in smoking and non-smoking young men. Infect Immun 1975; 12: 550-5.
11. James AL, Knuiman MW, Divitini ML, Musk AW, Ryan G, Bartholomew HC. Associations between white blood cell count, lung function, respiratory illness and mortality: the Busselton Health Study. Our Respir J 1999; 13: 1115-9.
12. Sparrow D, Glynn RJ, Cohen M, Weiss ST. The relationship of the peripheral leukocyte count and cigarette smoking to pulmonary function among adult men. Chest 1984; 86: 383-6.

13. Chan-Yeung M, Abboud R, Dy Buncio A, Vedel S. Peripheral leucocyte count and longitudinal decline in lung function. Thorax 1988; 43: 462-6.
14. Gillum RF. Peripheral leucocyte count and pulmonary function in a national sample of women and men. Ann Epidemiol 1991; 1: 525-31.
15. Neas LM, Schwartz J. The determinants of pulmonary diffusing capacity in a national sample of U.S. adults. AM J Respire Crit Care Med 1996; 153: 656-64.
16. Schwartz J, Weiss ST. Peripheral blood leucocyte count and respiratory symptoms. Ann Epidemiol 1993; 3: 57-63.
17. Schnack Ch, Festa A, Schwarzmaier-D'Assie A, Haber P, Schernthaner G. Pulmonary dysfunction in type 1 diabetes in relation to metabolic long-term control and to incipient diabetic nephropathy. Nephron 1996; 74: 395-400.
18. Davis TM, Knuiman M, Kendall P, Vu H, Davis WA. Reduced pulmonary function and its associations in type 2 diabetes: the Fremantle Diabetes Study. Diabetes Res Clin Pract 2000; 50: 153-9.
19. Sinha S, Guleria R, Misra A, Pandey RM, Yadav R, Tiwari S. Pulmonary function in patients with type 2 diabetes mellitus & correlation with anthropometry & microvascular complications. Indian J Med Res 2004; 119: 66-71.
20. Sandler M, Bunn AE, Stewart RI. Cross-section study of pulmonary function in patients with insulin-dependent diabetes mellitus. Am Rev Respir Dis 1987; 135: 223-9.
21. Ljubic S, Metelko Z, Car N, Roglic G, Drazic Z. Reduction of diffusion capacity for carbon monoxide in diabetic patients. Chest 1998; 114: 1033-5.
22. Asanuma Y, Fujiya S, Ide H, Agishi Y. Characteristics of pulmonary function in patients with diabetes mellitus. Diabetes Res Clin Pract 1985; 1: 95-101.
23. Shah SH, Sonawane P, Nahar P, Vaidya S, Salvi S. Pulmonary function tests in type 2 diabetes mellitus and their association with glycemic control and duration of the disease. Lung India 2013; 30: 108-12.
24. Borst BB, Gosker HR, Zeegers MP, Schols AM. Pulmonary function in diabetes: A metaanalysis. Chest 2002; 138: 393-406.
25. Engstrom G, Janzon L. Risk of developing diabetes is inversely related to lung function: a population-based cohort study. Diabetic Med 2002; 19: 167-70.
26. Lawlor DA, Ebrahim S, Davey Smith G. Associations of measures of lung function with insulin resistance and type 2 diabetes: findings from the British Women's Heart and Health Study. Diabetologia 2004; 47: 195-203.
27. Lange P, Parner J, Schnohr P, Jensen G. Copenhagen City Heart Study: longitudinal analysis of ventilatory capacity in diabetic and non diabetic adults. Eur Respir J 2002; 20: 1406-12.

Obstetric Admissions to the Intensive Care Unit in Malta (2012-2015): a nationwide, population-based, cohort study

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Abstract

Introduction: A retrospective review of obstetric admissions to Malta's ICU during a four-year period was planned. Comparison to similar studies was used to benchmark the local situation.

Method: Patients were recruited using the ICU admissions database between 2012 and 2015. Patients admitted for obstetric pathology at any stage of pregnancy and up to 30 days postpartum were included and medical notes reviewed retrospectively. Data collected included demographics, ICU admission diagnosis, management including surgery, length of ICU and hospital stays, and maternal and neonatal outcomes. Data was analysed using MS Excel®.

Results: 42 patients were admitted to ICU for an obstetric pathology over the four-year period; 39 were included in the study. 0.25% of obstetric deliveries needed admission to ICU and obstetric admissions accounted for 0.87% of all ICU admissions. The commonest admission diagnosis was haemorrhage (62%), followed by hypertensive diseases of pregnancy (HDoP; 26%) and sepsis (23%). All patients had an arterial line inserted and this represented the only intensive management for one third of patients. 26 patients (67%) required surgery - the commonest procedure was an emergency Lower Segment Caesarian Section. There were no maternal deaths; however, four patients miscarried and there were three perinatal deaths.

Conclusions: The percentage of deliveries requiring ICU admission in Malta is in line with internationally-reported rates. Obstetric admissions as a percentage of all ICU admissions were lower than the reported averages in the literature. The most common admission diagnosis was haemorrhage, in contrast to most other studies where admission was due to HDoP.

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Introduction

Malta is an independent European island nation with a population of just over 400,000.[1] There is one main acute public hospital, Mater Dei Hospital (MDH), which houses a twenty-bed intensive care unit (ICU). There are no formal, separate high dependency units. The ICU caters for all medical and surgical patients above three years of age requiring high dependency (Level 2) or intensive care (Level 3). Children younger than three years go to the Neonatal and Paediatric Intensive Care Unit. The only other category of patients excluded is those post cardiac surgery, who are admitted directly to a Cardiac Intensive Care Unit post operatively. Due to this, ICU beds are a limited and sought-after resource in Malta.

The aim of this study was to perform a retrospective review of obstetric admissions to our ICU during a four year period (2012 – 2015). This was done to benchmark our current admission rate and utilization of Intensive Care services by the obstetric patient population. The data will be used to plan resource allocation, education and training, as well as to identify potential improvements in workflow, treatment and management. Comparison to similar studies performed in other countries will be done to review similarities and differences with the situation in Malta.

Materials and Methods

Permission to carry out the study was granted by the Chairperson of the Department of Anaesthesia and Intensive Care, the Director of the Department of Obstetrics and Gynaecology and the Data Protection Officer, all at Mater Dei Hospital. The audit was also approved by the University of Malta Research Ethics Committee (protocol code MD30/2016).

Patients were recruited by going through the ICU admissions database for the years 2012 to 2015 (four years in total) and listing those who were admitted to the ICU for an obstetric pathology at any stage of their pregnancy and up to 30 days postpartum. Medical notes were requested and reviewed retrospectively. Data collection sheets were designed by performing a literature review and noting what data was collected in similar, published studies. These were used for standardized data collection. The data collected included patient demographics, obstetric history, reason for admission to ICU, management including the need for surgery, length of ICU and hospital stays and maternal and neonatal outcome. Data was inputted into a MS Excel® spreadsheet and analysed using the same programme.

Results

There were 42 patients who were admitted to ICU at MDH for an obstetric pathology over the four year period; 39 of these were included in the study. The remaining three patients could not be included as the medical records of one could not be found, of one were found but were empty, and the third had the wrong reference number listed in the ICU database. Over the four year period, 0.25% of obstetric deliveries needed admission to ICU. Obstetric admissions accounted for 0.87% of all ICU admissions.

Average maternal age was 28.95 years and 62% of patients were in the 21 to 30 year age group when the admission to ICU occurred. Regarding ethnicity, the absolute majority were Caucasian (*n*=31; 79%). 15 women were in their first pregnancy (38%); 11 in their second (28%); and 13% of patients (*n*=5) were in their third or higher pregnancy. The commonest gestational age at which the obstetric event occurred was from the "thirty-third to the thirty-seventh week of pregnancy" (*n*=13; 33%), closely followed by "at more than thirty-seven weeks gestation" (*n*=12; 31%). There were five patients who were admitted to ICU postpartum and one patient required admission after embryo transfer as part of an assisted-fertility procedure. This intervention did result in a pregnancy that was unfortunately miscarried a few days after discharge from ICU.

The commonest admission diagnosis by far that warranted an ICU admission was haemorrhage (*n*=24; 62%), followed by hypertensive diseases of pregnancy (*n*=10; 26%) and sepsis (*n*=9; 23%). Some patients had more than one diagnosis at the time of admission. All patients had an arterial line inserted on admission to ICU and this represented the only intensive management for a considerable proportion of this cohort (*n*=13; 33%). 18 patients (46%) required ventilatory support. This number includes patients who were admitted intubated and mechanically ventilated and were transferred to ICU for weaning and extubation. 8 patients (21%) required infusions of vasoactive drugs, two (5%) required renal replacement therapy by CVVHDF (Continuous Veno-Venous HaemoDiaFiltration) and one patient (2.5%) needed pituitary hormone supplementation.

26 patients (67%) required surgery as part of their treatment and the commonest procedure carried out was an emergency LSCS (Lower Segment Caesarian Section). The absolute majority of patients (*n*=19; 73%) received a general anaesthetic for their surgeries. Four of these had their procedure started under neuro-axial block and were then converted to a general anaesthetic (15%).

In terms of length of ICU stay, 12.8% of patients stayed less than 24 hours. 24 patients (61.5%) stayed between one and two days. 6 patients stayed 3-5 days, 3 patients for 6-10 days and 1 patient stayed for longer than 10 days. Regarding total hospital stay, 8 patients stayed 5

days or less (20.5%), 12 patients stayed between 6 and 10 days (30.8%) and 19 patients stayed more than 10 days (48.7%).

We also looked at records of contact with the neonate, breast milk expression, ice pack application to breasts and prescriptions of dopamine antagonists. In 10 patients (25.6%), these observations were not applicable (e.g. early pregnancy miscarriage). In 25 patients (64.1%), no documentation of the above was found. No patient was prescribed or given dopamine antagonists at any point.

Where documentation was present and applicable, breast milk expression was recorded for 2 patients (5.1%), breast milk expression and contact with neonate was recorded for 1 patient (2.6%) and contact with neonate and ice packs to breasts were recorded for 1 patient (2.6%).

There were no maternal deaths over this period. However, four patients miscarried their pregnancy and there were three perinatal deaths.

Discussion

In Malta, 0.25% of all deliveries required ICU admission and obstetric patients represented 0.87% of all intensive care unit admissions. In developed countries, 0.07-0.9% of pregnant women require ICU admission, accounting for up to 3% of ICU admissions overall.[2-3] Therefore, our average for percentage of the obstetric population requiring ICU admission falls into the described range, but compared to the reported 3% of ICU admissions overall, our obstetric population accounted for only 0.87% of ICU admissions.

This is quite an unexpected finding considering that no formal HDU (level 2) facilities exist at MDH and our ICU admits patients requiring Level 2 and Level 3 care. In spite of this, our obstetric admission rate when compared to total ICU admissions is about a third lower than reported in previous studies. Although ICU beds are a limited resource, it is very unlikely that obstetric patients requiring Level 2 or Level 3 care were refused admission due to lack of bed space. This is the only ICU on the island and so patients could not be transported to another location. Similarly low rates of obstetric admissions as a percentage of total ICU admissions have been previously reported by a study from The Netherlands published in 2006[4] from a tertiary care centre, where the rate was found to be 0.7%.

Regarding the admission diagnoses, the commonest in our cohort were: 62% haemorrhage, 26% hypertensive disorders of pregnancy and 23% sepsis. A literature review for similar studies identified eleven studies (Table 1). From these, the most frequent ICU admission diagnosis in obstetric patients is hypertensive disorders of pregnancy (HDoP) as outlined in Table 1. We believe the relatively low percentage of ICU admissions for HDoP in Malta is due to the fact that most patients with pregnancy induced hypertension and mild-moderate pre-eclampsia are managed on the labour ward by the obstetricians. Patients with moderate-severe pre-eclampsia or eclampsia are referred to ICU for management of intractable hypertension despite IV agents; seizure control; or to manage complications such as HELLP syndrome, DIC and intracranial haemorrhage.

All patients admitted to ICU had an arterial line inserted for invasive blood pressure monitoring and regular blood-letting. In 33% of our patients, this was the only intensive care intervention. It could be argued that these patients could be managed in an Obstetric High Dependency Unit (HDU), thus reducing the workload, cost and psychological sequelae associated with ICU admission. A paper by Zeeman GG et al[14] proposes general recommendations for the organization of obstetric critical care including the Obstetric Intermediate Care Unit and medical/ surgical intensive care units. This could be relevant and helpful to the Maltese scenario due to the limited number of intensive and high dependency care beds. The findings regarding length of ICU admission, i.e. 29 patients (74.3%) stayed two days or less, may also be indicative of less severe, or quickly resolving, pathology that could be successfully and safely managed in an HDU setting.

We noted poor documentation regarding additional specific obstetric issues, for example, contact with the neonate, breast milk expression and ice-pack application to breasts. We feel this is an opportunity for improvement in our ICU care, or at least, an opportunity to enhance documentation. These care points may be overlooked in a busy ICU setting that does not frequently admit obstetric patients and so increased input from obstetricians and midwives may be relevant in these situations. We are very pleased to note the 0% maternal mortality rate in Malta for the years 2012 to 2015.[15]

***Table 1**: Commonest ICU admission diagnoses for obstetric patients*

Year of Publication	Authors	Country	Most common admission diagnosis	Second most common admission diagnosis	Third most common admission diagnosis
1996	Bouvier-Colle MH et al [5]	France	HDoP 26.2%	Haemorrhage 20%	Embolisms 12.4%
2001	Quah TCC et al [6]	Singapore	HDoP 50%	Haemorrhage 24%	Neurological 11%
2003	Demirkiran O et al [7]	Turkey	HDoP 73.6%	Haemorrhage 11.2%	Infection 2.4%
2004	Mirghani HM et al [8]	United Arab Emirates	Haemorrhage 28.4%	HDoP 25%	Cardiac problems 21.6%
2004	Okafor UV et al [9]	Nigeria	HDoP 56%	Haemorrhage 22.2%	N/A
2006	Keizer JL et al[4]	The Netherlands	HDoP 21-76%	Haemorrhage 15-33%	Miscellaneous 13.4%
2010	Zwart JJ et al[10]	The Netherlands	Haemorrhage 48.6%	HDoP 29.3%	Sepsis 8.1%
2011	Crozier TM et al [3]	Australia	Haemorrhage 33%	HDoP 15%	Cardiac disease 13%
2011	Gupta S et al [11]	India	Haemodynamic instability 83%	Respiratory insufficiency 12.54%	Neurological dysfunction 4.16%
2015	Ruimy A et al[12]	France	HDoP 64%	Haemorrhage 16.7%	Miscellaneous disorders 5.4%
2016	Seppanen P et al [13]	Finland	HDoP 57%	Haemrrohage 25.4%	N/A

HDoP – Hypertensive Disorders of Pregnancy

Our study has some limitations. Only 93% of obstetric admissions to ICU during this four year period were analyzed (39/42). The rest could not be included due to lack of proper documentation or misplacement of patient notes. Patients may also have been missed due to erroneous entries into the ICU admission database. This source of error was minimized by looking at both admission diagnosis and the specialty of the caring consultant (all admissions by obstetric consultants were reviewed for inclusion). It is however possible a very small number of patients were missed.

In conclusion, the percentage of all deliveries requiring ICU admission in Malta is similar to rates previously reported from other countries. The percentage of obstetric patients as part of all intensive care unit admissions is lower than the reported averages in the literature. Despite this, due to the limited number of ICU beds available, an HDU set up may help to reduce the number of obstetric admissions to ICU even further. We feel there is a need for improved documentation, and possibly in points of care, with respect to specific obstetric issues e.g. neonatal contact and breast care. The mortality rate of 0% over these four years is an achievement.

Summary Box

What is already known about this subject?

- Rate of obstetric admissions to ICU as a percentage of all deliveries in developed countries is reported at 0.07-0.9% [2-3]
- Rate of obstetric admissions to ICU as a percentage of all ICU admissions in developed countries is reported as up to 3% [2-3]
- The commonest ICU admission diagnosis in obstetric patients from the literature is hypertensive disorders of pregnancy (Table 1)

What are the new findings?

- Rate of obstetric admissions to ICU as a percentage of all deliveries at MDH – 0.25%
- Rate of obstetric admissions to ICU as a percentage of all ICU admissions at MDH – 0.87%
- Identification of haemorrhage as the most common admission diagnosis in obstetric patients in ICU at MDH
- Level and frequency of intensive care interventions in obstetric patients admitted to ICU at MDH

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References

1. National Statistics Office, Valletta, Malta. Census of Population and Housing 2011 Preliminary Report. 2012.
2. Germain S, Wyncoll D, Nelson-Piercy C. Management of the critically ill obstetric patient. Curr Obstet Gynaecol. 2006; 16:125–33
3. Crozier TM, Wallace EM. Obstetric admissions to an integrated general intensive care unit in a quaternary maternity facility. Aust NZ J Obstet Gyn. 2011; 51: 233-8
4. Keizer JL, Zwart JJ, Meerman RH, Harinck BIJ, Feuth HDM, van Roosmalen J. Obstetric intensive care admissions: A 12-year review in a tertiary care centre. Eur J Obstet Gynecol Reprod Biol. 2006; 128: 152-156
5. Bouvier-Colle MH, Salanave B, Ancel PY et al. Obstetric patients treated in intensive care units and maternal mortality. Eur J Obstet Gynecol Reprod Biol. 1996; 65: 121-5
6. Quah TCC, Chiu JW, Tan KH, Yeo SW, TAN HM. Obstetric Admissions to the Intensive Therapy Unit of a Tertiary Care Institution. Ann Acad Med Singapore. 2001; 30: 250-3
7. Demirkiran O, Dikmen Y, Utku T, Urkmez S. Critically ill obstetric patients in the intensive care unit. Int J Obstet Anest. 2003; 12: 266-270
8. Mirghani HM, Hamed M, Ezimokhai M, Weerasinghe DSL. Pregnancy-related admissions to the intensive care unit. Int J Obstet Anesth. 2004; 13:82-5
9. Okafor UV, Aniebue U. Admission pattern and outcome in critical care obstetric patients. Int J Obstet Anesth. 2004; 13: 164-6
10. Zwart JJ, Dupuis JRO, Richters A, Ory F, van Roosmalen J. Obstetric intensive care unit admission: a 2-year nationwide population-based cohort study. Intens Care Med. 2010; 36: 256-63
11. Gupta S, Naithani U, Doshi V, Bhargava V, Vijay BS. Obstetric critical care: A prospective analysis of clinical characteristics, predictability and fetomaternal outcome in a new dedicated obstetric intensive care unit. Indian J Anaesth. 2011 Mar –Apr; **55** (2): 146-53
12. Ruimy A, Calon B, Guillaume A et al. Obstetric intensive care unit admission: a six year cohort study. Intens Care Med Experimental. 2015; 3 (Suppl 1): A525
13. Seppanen P, Sund R, Roos M et al. Obstetric admissions to ICUs in Finland: A multicentre study. Intens Crit Care Nur. 2016; 35: 38-44
14. Zeeman GG, Wendel Jr GD, Cunningham FG. A blueprint for obstetric critical care. Am J Obstet Gynecol. 2003; 188:532-6
15. National Obstetric Information System (NOIS) Reports 2012, 2013, 2014, 2015 issued by the Department of Health Information and Research, Government of Malta

Original Article

Bilateral breast reduction surgery at Mater Dei Hospital: Analysis of physical and psychological symptoms using the BREAST- Q

Juanita Parnis, Duncan Aquilina, Matthew Borg, Francis X. Darmanin, Joseph E. Briffa

Abstract

Introduction: The literature describes a high patient satisfaction rate after breast reduction. In this retrospective study, we used the BREAST-Q to analyze satisfaction with breast appearance and physical, psychosocial and sexual well-being of patients who underwent bilateral breast reduction (BBR) at Mater Dei Hospital (MDH). This was done to obtain local data which was totally lacking. With a quantitative value, we were able to compare our results with other centers worldwide and have a baseline for future work. We also looked into whether age, co-morbidities and weight of breast tissue removed makes a difference to the overall satisfaction rate.

Method: We hope to demonstrate a better quality of life following surgery and aim to compare the results of this study to others carried out worldwide. In this way we can better understand the local situation and see where there is the room for improvement. Permission to use the BREAST-Q questionnaire and translate it into Maltese was obtained from Mapi Reasearch Trust. The questionnaire was offered either in Maltese or in English, after an official translation was produced following a linguistic validation process. All patients who underwent BBR at MDH under the care of both consultant Plastic Surgeons were invited to complete the BREAST-Q questionnaire via a telephone call and asked to come to MDH to fill it in. Other patient specific information was obtained from their hospital notes.

Results: Our study had a response rate of 91% i.e. a total of 39 patients. The average patient was 44 years of age. Over the years, there was an overall increase in BBR surgeries, with July and October being the commonest months. Hypertension was the commonest co-morbidity and 1-2 kg of tissue was removed during most of the operations. Our study compared well with results from Ohio. On the whole, younger patients are more satisfied after surgery and the amount of tissue removed does not seem to make a difference to overall satisfaction.

Conclusion: In this world of evidence-based medicine, the BREAST-Q is ideal for a holistic approach in analyzing patient satisfaction after BBR. Having local data at hand makes it easier for patients who are interested in undergoing the surgery to associate themselves with other local individuals.

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Keywords

Breast, Personal Satisfaction, Physical Appearances, Psychology

Introduction

Bilateral breast reduction is well known for the benefits it provides to patients who decide to have the surgery. It is usually performed to improve the symptoms of macromastia including intertriginous infections, back and shoulder pain, dissatisfaction with breast appearance, poor sexual and psychosocial well-being amongst others.[1-2,4-5,8-10] Although a high degree of satisfaction and improvement in quality of life have been reported previously in the literature, few studies have used reliable and validated survey instruments. The BREAST-Q is the only questionnaire to assess breast reduction outcomes that meets international and federal standards for questionnaire development while measuring a variety of outcomes, including satisfaction with breasts and overall outcome, psychosocial, sexual and physical well-being and satisfaction with care. [3] In this retrospective study, we have looked into all the cases of patients who had bilateral breast reduction at Mater Dei Hospital, Malta using the post-operative section of the Bilateral Breast Reduction BREAST-Q questionnaire. This was done to obtain local data regarding patient satisfaction with the surgeon, nursing and clerical staff, the surgery itself and overall satisfaction, which was totally lacking. This data can also be used as a baseline for future work. By using the BREAST-Q, we were able to compare our results with other centers. We have also looked into whether age, co-morbidities and the weight of breast tissue removed in each patient, makes a difference to the overall satisfaction rate.

Method

Permission to carry out this audit was first obtained from the two Plastic Surgeons working at MDH and from the Chairperson of surgery. Permission to use the BREAST-Q questionnaire in English was obtained from Mapi research Trust. We also obtained permission to translate the questionnaire into Maltese. In order to do so, we had to go through a linguistic validation process so that the translation is an official one. An invitation letter and a consent form for the patients were also produced in Maltese and in English. Permission was then obtained from the Data protection Unit at MDH.

All the patients who had BBR at MDH since it opened its doors were included in the audit. This included patients from 2008 up to May 2015. All the patients were at least 6 weeks post-surgery. They were contacted via a telephone call and invited to take part in the audit. The patients were then asked to either come to MDH to fill in the questionnaire or it was sent to them by post, providing also a self-addressed envelope. The questionnaire was offered to them either in Maltese or in English and it included an invitation letter and a consent form in addition to the questionnaire. Telephone call reminders were done to follow up questionnaires sent by post. The results were inputted into the BREAST-Q scoring software: the Q score, and results were obtained. The age of the patient when they had the surgery, the total weight of breast tissue removed, smoking history and co-morbidities were obtained from the patients' hospital notes and were coded and analyzed using MS Excel®.

Results

Forty three patients underwent a bilateral breast reduction under the care of both consultant Plastic Surgeons since the opening of Mater Dei Hospital in 2008 up to May 2015. Of these patients, 39 (91%) completed the BREAST-Q post-operative breast reduction questionnaire.

From a total of 43 patients, the notes of 41 patients were available to be reviewed. The average age at which the patients had their surgery was 44 years, ranging from 19 to 67 years as shown in figure 1. Figure 2 and 3 shows the number of breast reduction surgeries done per year and the month in which they were done respectively. Patient co-morbidities are shown in figure 4. The average weight of breast tissue removed from each patient was 2kg. Total weight of breast tissue removed from each patient varied between 0.328 kg and 6.353 kg, as shown in figure 5. Twenty nine patients (71%) were non-smokers, eight patients (20%) were ex-smokers and 4 patients (10%) were smokers.

***Figure 1**: Number of patients per age group*

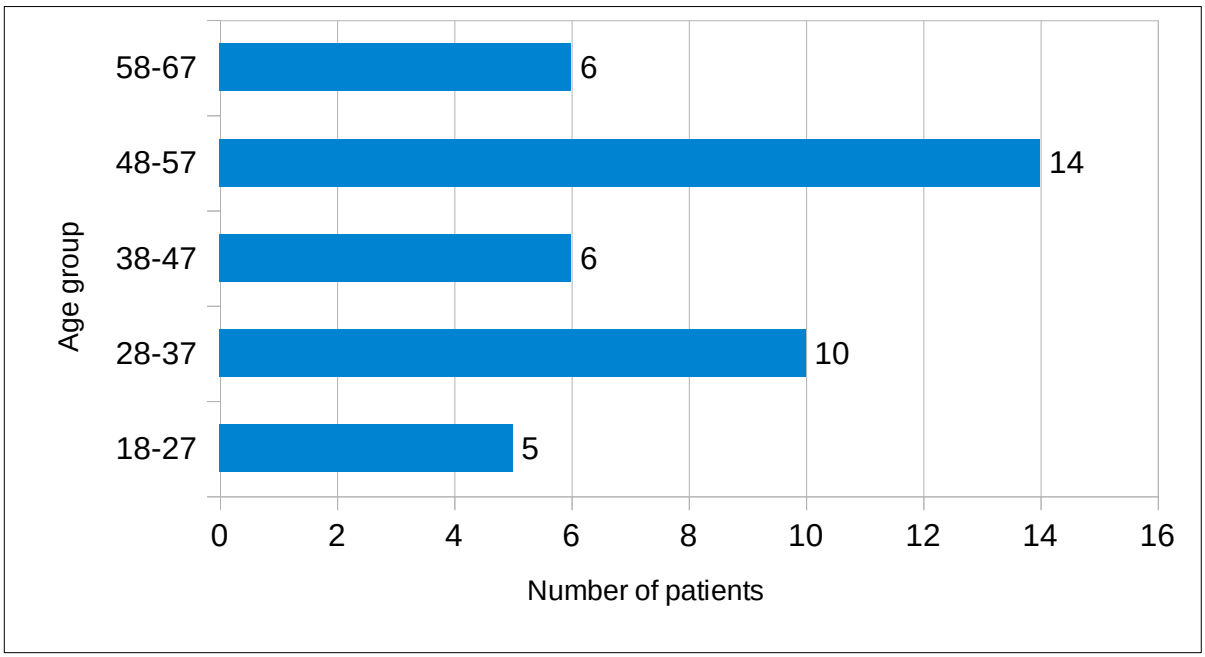


***Figure 2**: Number of surgeries per year*

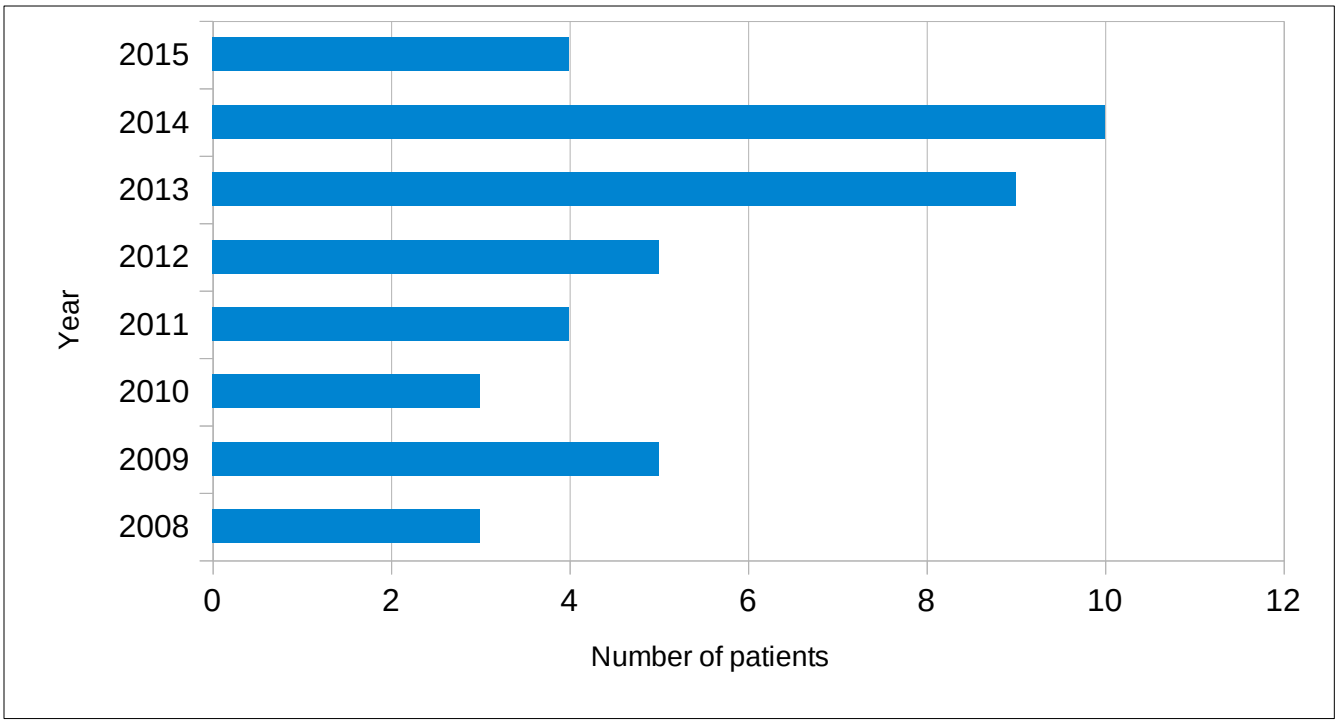


Figure 3: *Number of surgeries in each month*

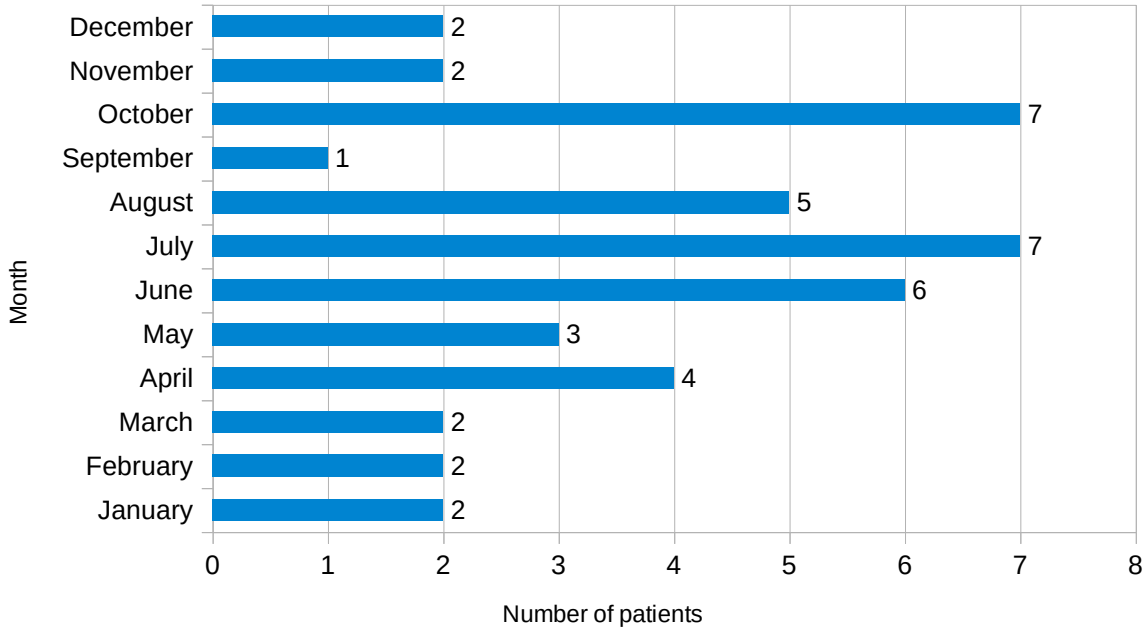


Figure 4*: Patient co-morbidities*

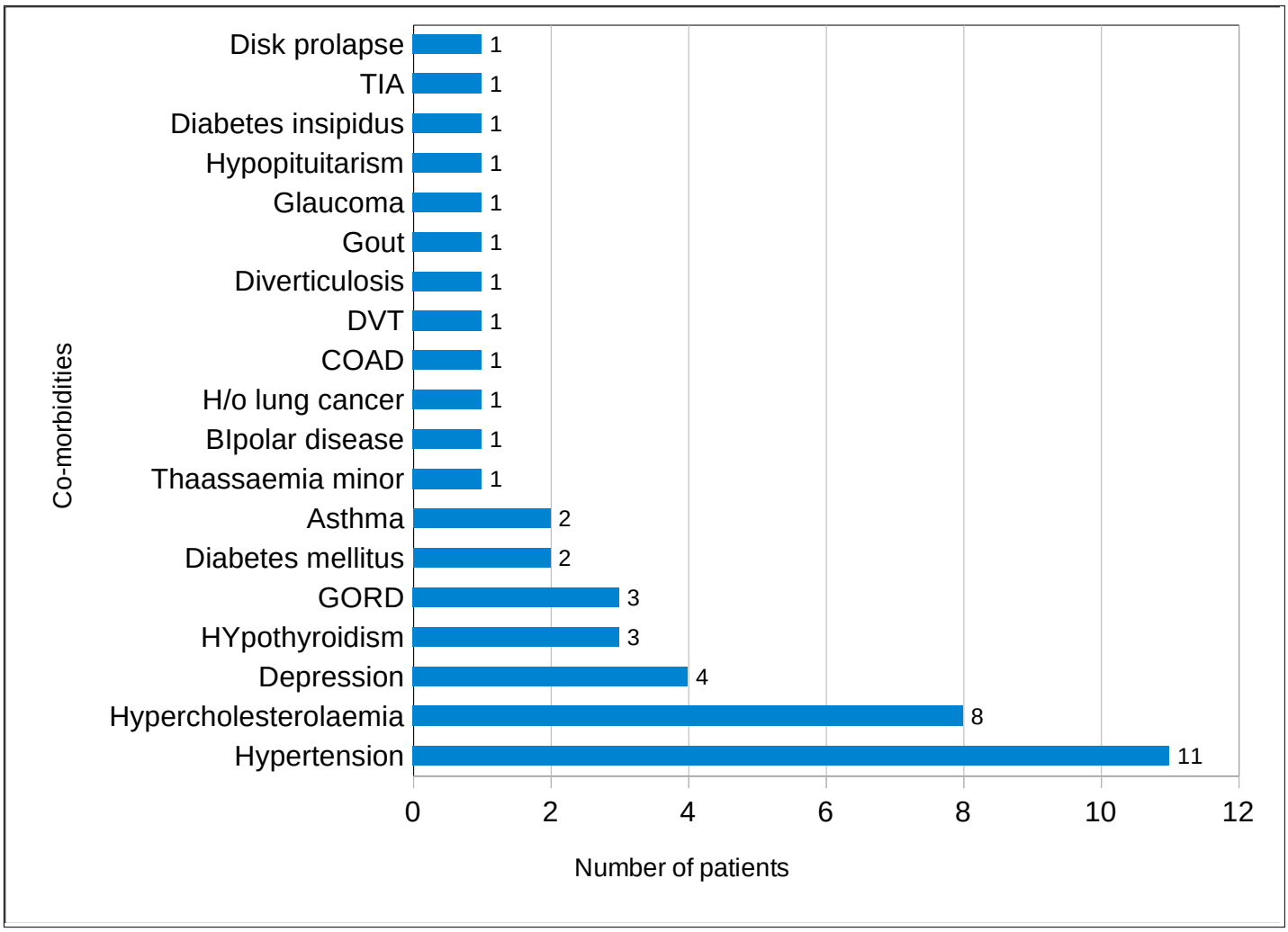
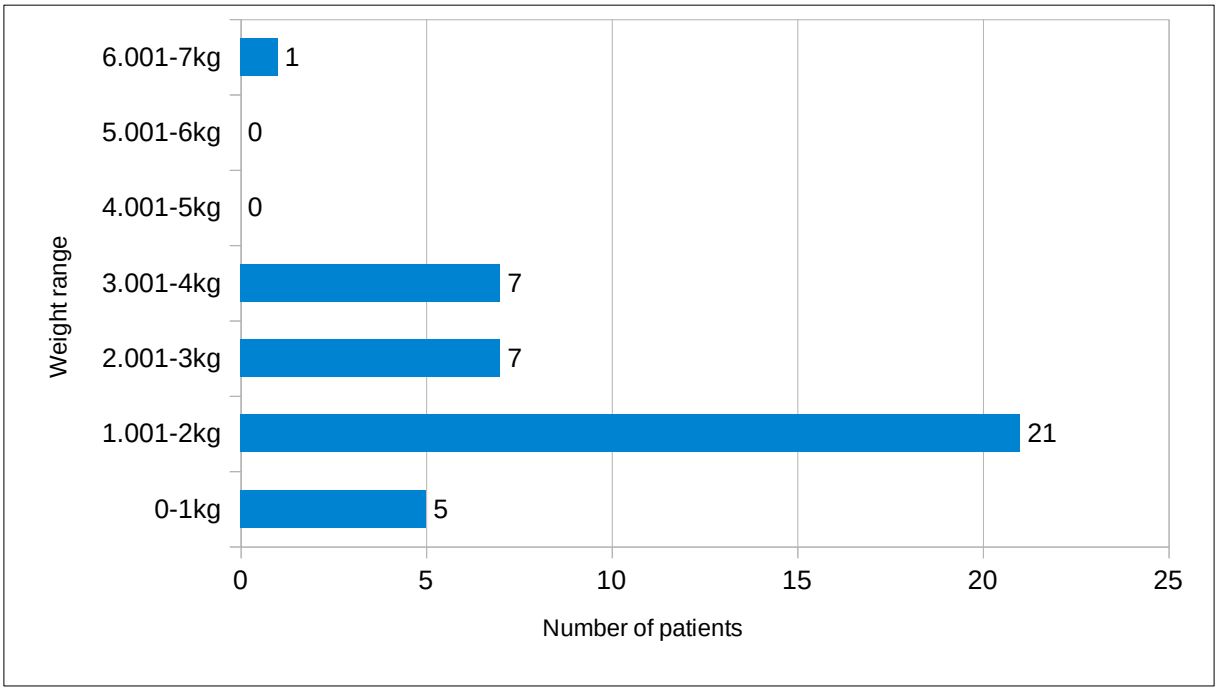


***Figure 5**: Weight of breast tissue removed per patient*



All BREAST-Q scores range from 0-100. A higher score means high satisfaction or better health related quality of life. The range and average patient satisfaction is shown in figure 6.

***Table 1**: Local BREAST-Q scores*

	Range	Average
Satisfaction with breasts	24 - 100	75
Satisfaction with outcome	41 - 100	91
Psychosocial well-being	34 - 100	79
Sexual well-being	21 - 100	73
Physical well-being	53 - 100	72
Satisfaction with information	48 - 100	77
Satisfaction with nipples	0 - 100	75
Satisfaction with surgeon	41 - 100	86
Satisfaction with medical staff	47 - 100	94
Satisfaction with office staff	26 - 100	95

Figure 6 shows the relation between the satisfaction with outcome of patients and their age and figure 7 shows the relation between the satisfaction with outcome of patients and the total amount of breast tissue removed.

***Figure 6**: The relation between age and patient satisfaction*

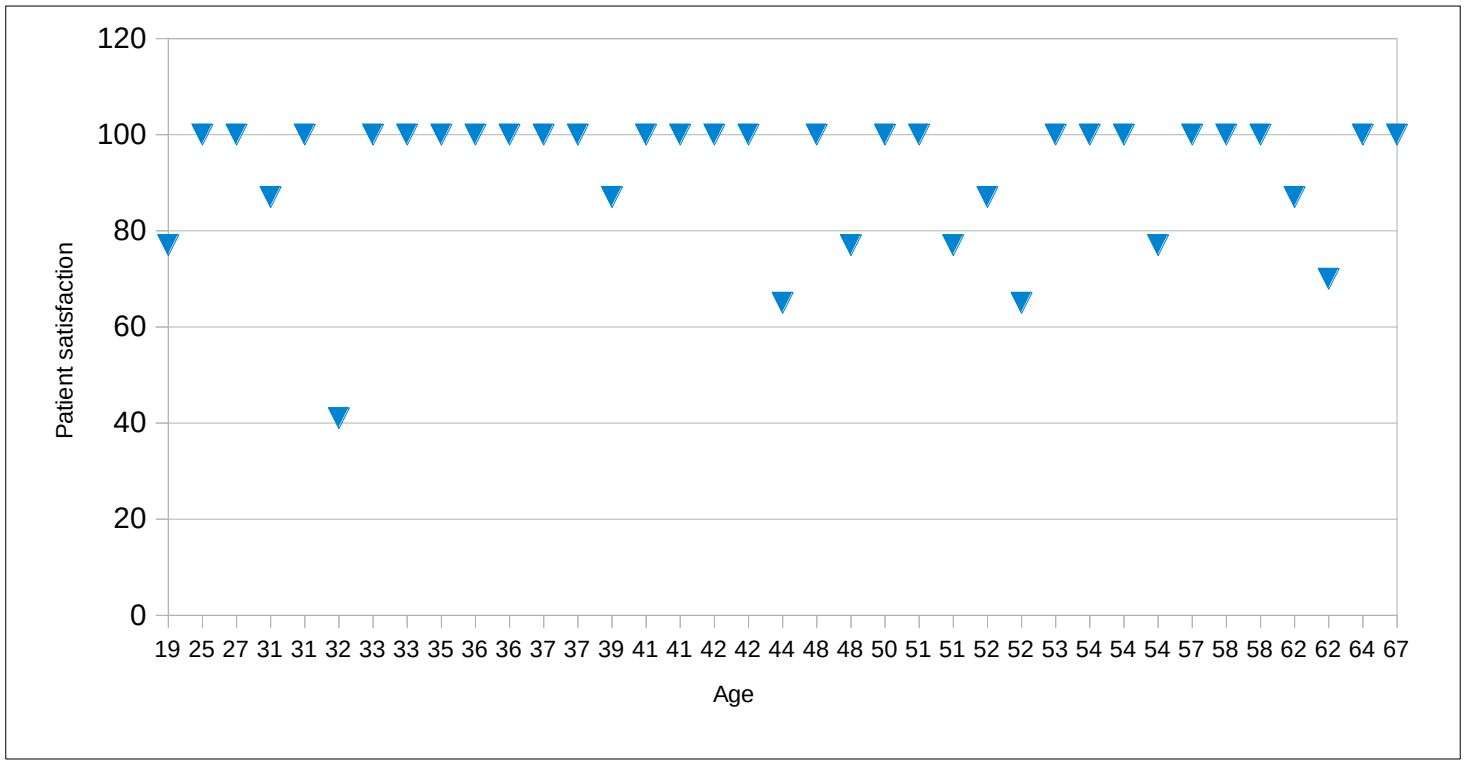
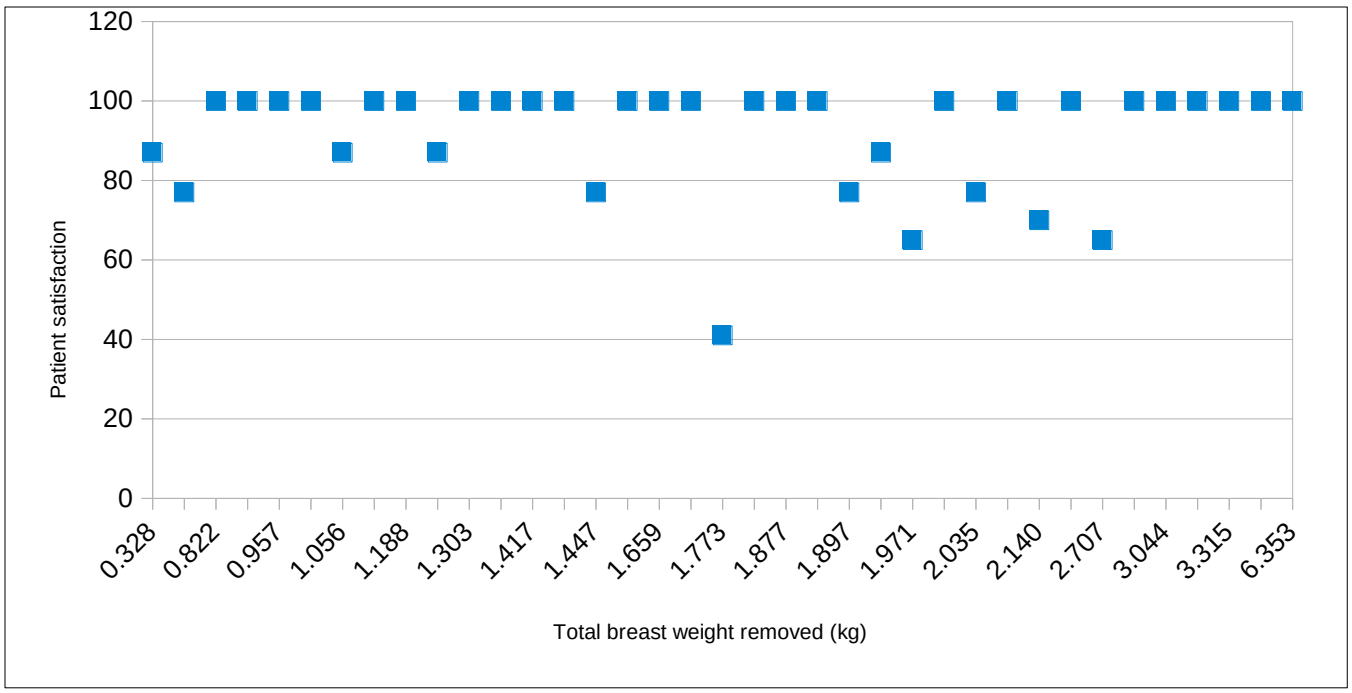


***Figure 7:** The relation between total amount of breast tissue removed and patient satisfaction*



Discussion

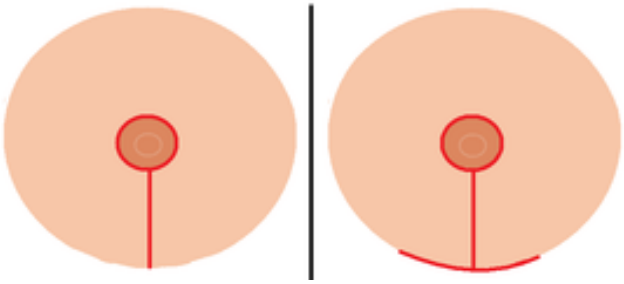
In the literature one can find multiple patient-reported outcome measures. The Short Form-36[4,8], Rosenburg Self-Esteem Scale[4-5,9], Breast-Related Symptoms Questionnaire, Brief Symptom Inventory [3] amongst others, have been used to show patient reported improvements in satisfaction and quality of life following breast reduction surgery. However, most of these instruments are generic rather than surgery specific and thus do not assess all important aspects of quality of life and satisfaction among patients who have had a breast reduction. [3] We decided to implement the BREAST-Q as our survey tool because during the development of the BREAST-Q, the questionnaire was tested and underwent psychometric analysis. In our retrospective study, the data compares well with the data obtained in the study from Ohio by Coriddi et al.

In our study, we had a 91% response rate. This might be because the patients were asked to take part by phone and non-responders were followed up. We made it easy for patients to reply by sending them a stamped self-addressed envelope. It shows that middle aged women were the ones that had BBR most frequently. This is probably because they are old enough to have older children that do not need constant support but young enough to benefit from the surgery. On the whole, there was an increase in surgeries every year. There is a drop in the year 2015 as the data was only collected till May. Summer months were the commonest months for breast reductions. This may be due to the fact that the women have less child related evening activities in the summer, they have more support or they have no work during the summer months. September was the least common month probably because of the children going back to school which involves a lot of work for the parents. Most commonly, about 1-2 kg of tissue was removed from the breast because only few women have very severe macromastia. The patients rated the overall outcome as being 91% as compared to the 75% regarding breast satisfaction. This might be due to the fact that the earlier patients did not really know what to expect from the surgery. This was improved by the introduction of the breast reconstruction nurse in our unit. The higher values were associated with satisfaction with hospital staff, confirming how important it is for the patients to feel valued and cared for when in hospital. The study could have been improved by giving a questionnaire to the patient before and after surgery to take into consideration differences in patients' perceptions. When comparing the age and amount of breast tissue removed with satisfaction, it seems that younger patients are generally happier and the amount of breast tissue removed does not make a huge impact on their satisfaction.

Breasts that are hypertrophic have an appearance that is frequently disliked by patients. Apart from the large size, these breasts can have a flat upper pole and various degrees of ptosis because of their weight. After a breast reduction, patients are generally happy with the new appearance of their breasts which are smaller and lifted. [3]

Macromastia can be due to either increased breast tissue, increased adipose tissue or a combination of both. Thus, patients should ideally have a normal BMI before having the surgery. All the patients at our unit have pre-operative photographs taken at the Medical Illustrations Department. Most of our patients had wise pattern incisions and only a few had a vertical incision breast reduction. This is because if a larger volume of breast tissue needs to be removed, a wise pattern incision is needed. Scars resulting from both surgeries are shown in figure 7. Free nipple grafts are usually done when the sternal notch to nipple length is more than 40cm or the distance from the inframammary fold to the nipple is more than 20cm. This is because there will not be enough blood supply to the nipple areolar complex and thus there is a high risk of post-operative soft tissue necrosis. An insensate nipple is the price to pay.

***Figure 8**: Incisions in vertical and wise pattern breast reductions*



During a breast reduction, the nipple areolar complex is raised on a pedicled flap, skin flaps are raised and excision of breast tissue carried out and sent for histology. Finally, the nipple is repositioned

at a higher level than it was before. Suturing is done using absorbable sutures to the dermis and subcuticular. Closed suction drains and antibiotics are almost always used in this cohort of patients in our unit. Complications of a breast reduction include seroma, haematoma, infection, fat necrosis, soft tissue necrosis, wound breakdown and scarring, nipple discolouration, and hypertrophic and painful scars, amongst others.

The Plastic Surgery Unit has introduced the service of a breast reconstruction nurse that meets the patients from their first encounter up to their last. The patients are counseled, shown videos and images regarding the surgery and are followed up by the breast reconstruction nurse till they are fully healed and can contact her should they have any concerns. The patients have mentioned that this service gives them a lot of reassurance and that they are very happy about the whole experience.

Conclusion

In this world of evidence-based medicine, the BREAST-Q is ideal for a holistic approach in analyzing patient satisfaction after BBR. In this study, we have shown satisfaction with breast appearance, psychosocial, physical and sexual well-being, satisfaction with information and with surgeon, nursing and clerical staff in our unit. Having local data at hand, makes it easier for patients who are interested in having the surgery to associate themselves with other local individuals.

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References

1. Blomqvist L, Eriksson A, Brandberg Y. Reduction Mammoplasty Provides Long-Term Improvment in Health Status and Quality of Life. Plastic and Reconstructive Surgery. Vol 106, No 5, 991-997.
2. Chao JD, Memmel HC, Redding JF, Egan L, Odom LC, Casas LA. Reduction mammoplasty is a functional operation, improving quality of life in symptomatic women: A prospective, single centre breast reduction outcome study. Plast Reconstr Surg. 2002; 110:1644-4652; discussion 1653.
3. Coriddi M, Nadeau M, Taghizadeh M, Taylor A. Analysis of Satisfation and Well-Being following Breast Reduction Using a Validated Survey Instrument: The BREAST-Q. Plast. Reconstr. Surg. 132: 285, 2013.
4. Hermans BJ, Boeckx WD, De Lorenzi F, Van Der Hulst RR. Quality of life after breast reduction. Ann Plast Surg. 2005; 55:227-231.
5. Mello AA, Domingos NA, Miyazaki MC. Improvement in quality of life and self-esteem after breast reduction surgery. Aesthetic Plast Surg. 2010; 34:59-64.
6. Pusic AL, Klassen AF, Scott AM, Klok JA, Cordeiro PG, Cano SJ. Development of a New Patient-Reported Outcome Measure for Breast Surgery: The BREAST-Q. Plast. Reconstr. Surg. 124: 345, 2009.
7. Rogliani M, Gentile P, Labardi L, Donfrancesco A, Cervelli V. Improvment of physical and psychological symptoms after breast reduction. Journal of Plastic, reconstructive & Aesthetic Surgery (2009) 62, 1647-1649.
8. Saariniemi K, Luukkala T, Kuokkanen H. The outcome of reduction mammoplasty is affected more by psychosocial factors than by changes in breast dimensions. Scand J Surgery. 2011; 100:105-109.
9. Sabino Neto M, Demattê MF, Freire M, Garcia EB, Quaresma M, Ferreira LM. Self-esteem and functional capacity outcomes following reduction mammoplasty. Aesthet Surg J. 2008; 28:417-420.
10. Scott GR, Carson CL, Borah GL. Maximising outcomes in breast reduction surgery: A review of 518 consecutive patients. Plast. Reconstr. Surg. 2005: 116:1633-1639; discussion 1640.

Original Article

Insulin prescription and administration and blood glucose monitoring at Mater Dei Hospital

Carol Cardona Attard, Rachel Agius, Alison Psaila, Stephen Fava

Abstract

Background: Incorrect insulin prescription and administration has been associated with substantial medication-related patient harm and mortality. We aimed to assess whether blood glucose was being monitored according to our local hospital protocol and whether insulin was being prescribed accurately by doctors and administered safely by nurses. Moreover, we evaluated whether education to nurses and doctors resulted in less insulin prescription and administration errors.

Methods: Inpatients on insulin in Mater Dei Hospital's medical wards were recruited. Data was collected from patients' files on errors in insulin prescription and on the timing of blood glucose monitoring and insulin administration in relation to meals. The first audit was carried out in 2013. A re-audit was carried out in 2017 following education to doctors and nurses and a change in the treatment chart format. The z-test was used to compare the two audits.

Results: On re-auditing, a significant improvement was noted in the timing of blood glucose monitoring and insulin administration in relation to meals, in the legibility of the insulin doses, 'Units' were more written in full and supplementary Actrapid® was more frequently prescribed where indicated. However, inappropriate omission of fixed insulin doses occurred more often, while written instructions by doctors on when to administer fixed insulin, including supplementary Actrapid®, were still lacking. Moreover, there was no improvement in adherence to the supplementary Actrapid® algorithm by nurses.

Conclusion: Further education and an improved treatment chart including hypo- and hyperglycaemia trouble-shooting guidelines are required to further reduce insulin prescription and administration errors.

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Key words

insulin; prescription errors; administration errors; blood glucose monitoring; education.

Introduction

Subcutaneous insulin is considered a high-alert inpatient medication by the Institute for Safe Medication Practices.[1] It has a narrow therapeutic index and thus requires accurate dose changes together with careful administration and regular monitoring.[2] In a review by *Cousins et al,* 16,600 incidents related to incorrect insulin prescription and administration were identified between November 2003 and November 2009. Twenty four

percent of these incidents resulted in patient harm. These incidents mainly occurred following the administration of the wrong insulin type, dose, frequency or strength, as well as inappropriate omission or delayed dosage, leading to insulin being administered at an incorrect time in relation to food. Moreover, the abbreviation of 'Units' to 'U' or 'IU' may be read as 0 or 10, especially in cases of poor handwriting, which can result in the administration of 10 or 100 times higher insulin doses.[3] Confusion between the different available insulins or administration of insulin meant for another patient can also result in dangerous blood glucose fluctuations.[4] Thus, although insulin can be a life-saving medication, it can also be life-threatening when used incorrectly.[5]

Insulin was reported to be implicated in 33% of medication error related mortality. Much of these insulin prescription and administration errors can be the result of illegible handwriting, heavy work-loads on doctors and nurses, impaired communication, unawareness of the importance and possible complications associated with the incorrect timing of insulin administration in relation to meals and of the need to keep blood glucose controlled, as well as the absence of back-up checking systems.[5]

According to our teaching hospital's clinical practice guideline relating to insulin administration, all diabetic patients on insulin admitted to hospital, should have their capillary blood glucose checked 30 minutes before each meal and at bedtime (10pm).[6] This is because Actrapid®, which is the short-acting human insulin available at Mater Dei Hospital, should be administered 30 minutes prior to a meal or a carbohydrate containing snack.[7] On the other hand, rapid-acting insulin analogues (such as Novorapid®) should be given immediately before or after a meal, but the dose may need to be adjusted according to the patient's capillary blood glucose level prior to the meal.[8] Basal insulins such as Insulatard® or long-acting insulin analogues e.g. insulin Glargine, do not need to be administered in relation to meals.[9, 10] However, when Insulatard® is mixed with Actrapid® to form biphasic insulin or Mixtard®, administration should occur 30 minutes before a meal.[11]

Our trust also has a supplementary Actrapid® algorithm available to nursing staff, which guides them in administering supplementary Actrapid® pre-meals and at bedtime when blood glucose monitoring (BGM) is greater than 8mmol/L. An algorithm for supplementary Actrapid® is assigned according to the patient's total daily dose of insulin or alternatively according to the patient's body weight.[6]

The aim of this audit was to assess whether BGMs were being checked according to our local Mater Dei hospital protocol and whether insulin was being prescribed accurately by doctors and administered safely by nursing staff. Moreover, we evaluated the use of supplementary Actrapid®, and whether this was being given in accordance to our local guideline. Another objective of this audit was to document any inappropriate insulin omission as well as resultant complications secondary to improper insulin prescription or administration. The re-audit aimed to assess whether educational sessions to both doctors and nurses led to a reduction of such errors in insulin prescription and administration.

Materials and Methods

The treatment charts of adult patients aged 18 years and over, who were admitted to any acute or general medical ward, were reviewed for possible inclusion in the audit. The inclusion criteria involved adult patients on any regular fixed doses of insulin. Patients who were on an intravenous insulin infusion were excluded. Each participant involved with data collection would review their allocated wards to include any newly admitted patients. The 1st audit was carried out over a 4-week period in 2013. The re-audit was carried out over a 12-week period in 2017 following educational sessions to both doctors and nurses.

The audit was carried out by all the authors of this manuscript together with the doctors mentioned in the acknowledgement section. A proforma was drawn up by one of the authors and this was then reviewed and endorsed by the supervising consultant. In addition to this, all doctors involved with data collection were asked to attend a briefing on the proforma to ensure conformity in the data collection process. The briefing was carried out by the most senior author participating in the audit. Educational sessions were given by the corresponding authors together with a diabetes specialist nurse after the results of the first audit were issued. These were one hourly one-time sessions, where all doctors and nurses working at Mater Dei hospital were invited to attend via emails from the respective associations. A new treatment

chart, with space available to write any important instructions for any prescribed drug, had also been issued prior to the re-audit. The same proforma was used for both audits.

The proforma consisted of six parts: the first section included demographic data of each patient recruited, including age, sex, type of diabetes and reason for admission. The second part was concerned with treatment, specifically the type of insulin the patient was on. In the third section details of insulin and supplementary Actrapid® prescription, including a correctly filled algorithm available in the patients' files, was audited. Correct insulin prescription involved writing insulin and dose correctly and legibly, 'Units' in full and clear instructions on when to administer insulin in relation to meals. This was in turn followed up by auditing whether BGM and insulin administration, including supplementary Actrapid®, was carried out in relation to meals according to the local protocol. Any inappropriate insulin omission was recorded. Insulin omission was taken as inappropriate if omitted following correction of hypoglycaemic episode[12] or if not given despite the patient having a BGM >4mmol/L and not nil by mouth in both cases. The last section included details about any complications, mainly hypoglycaemia (BGM <4mmol/L)[12] or hyperglycaemia (BGM persistently >10mmol/L),[13] that might have arisen from errors of insulin prescription and administration.

The results were tabulated using an Excel® spreadsheet and expressed as absolute numbers and percentage values with the help of Microsoft Excel®. When comparing the results between the two audits the z-test was used. The International Business Machines Corporation Statistical Package for the Social Sciences programme was utilized for this purpose. A *p*-value of <0.05 was used to define statistical significance.

Permission from all consultants who were directly responsible for the management of these patients was obtained as well as approval from the data protection officer in order to access the patients' files. Ethics approval was not sought as at no point did any of the participants have any form of contact with the recruited patients.

Results

One hundred and five insulin-treated patients with diabetes admitted to 19 medical wards at Mater Dei Hospital were recruited during the original audit, while 150 patients were recruited during re-audit. Demographic data and treatment with different insulin regimes for both audit samples are shown in table 1 and figure 1 respectively.

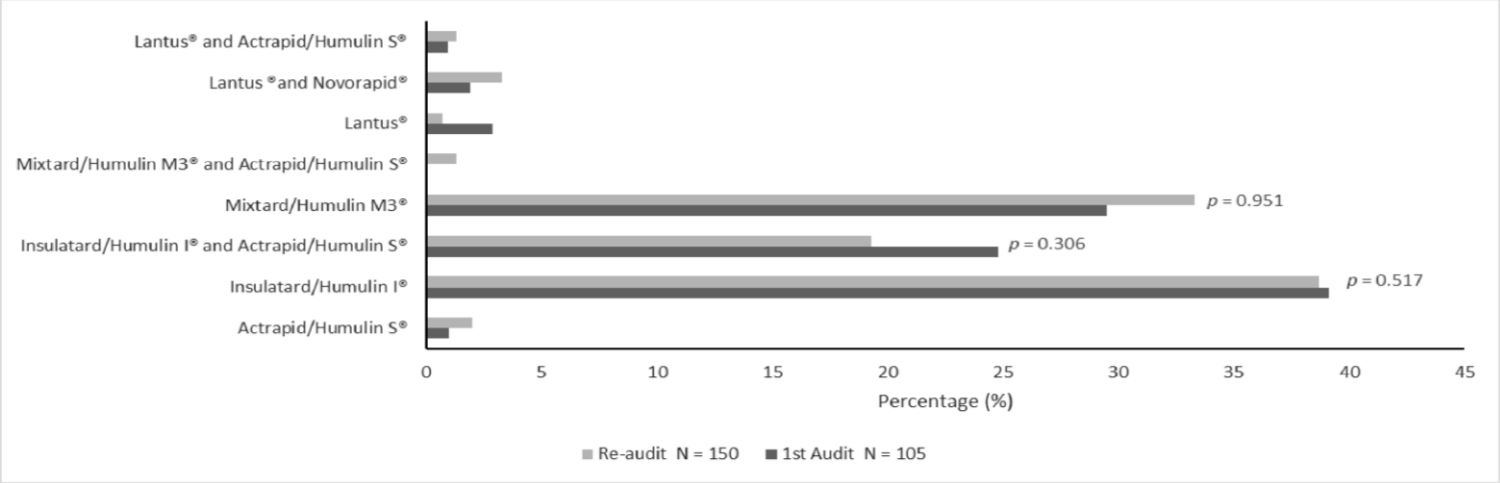
Table 1: *Demographic characteristics and frequency of patients in 1st audit and re-audit*

Demographic characteristics	***1st Audit (N = 105)***	***Re-audit (N = 150)***	***P*** [a]
Age, mean ± SD	69 ± 13.7	71.8 ± 12.5	0.15
Gender			0.869
No. female	55	77	
% female	52.4	51.3	
Type of Diabetes Mellitus			0.146
No. T1DM	10	7	
% T1DM	9.5	4.7	
No. T2DM	95	143	
% T2DM	90.5	95.3	

[a] z-test

SD- standard deviation; No- Number; %- percentage; T1DM- type 1 diabetes; T2DM- type 2 diabetes.

***Figure 1**: Different insulin regimes in 1st audit and re-audit*



Insulin prescription errors

A satisfactory result in writing the insulin name correctly and legibly was present in both audits, while an improvement in dose legibility was noted in the re-audit (see table 2). A significant improvement in writing 'Units' in full rather than abbreviated 'U' was recorded compared to the original audit (23.8% in 2013 to 41.3% in 2017, p=0.002). Moreover, supplementary Actrapid® was prescribed more often (74.8% in 2013 to 85.5% in 2017, p=0.002). However, no improvement in the prescription of insulin or supplementary Actrapid® in relation to meals was observed despite education and the launch of a new treatment chart in 2016.

BGM and insulin administration

BGM was carried out in all patients except for one patient in the re-audit. Capillary blood glucose was monitored at the correct time in relation to meals in 39% of patients during the initial audit (Table 3). This improved to 61.3% in the re-audit (p=<0.001).

Time of administration of insulin was charted in 97.3% in the re-audit, which is a significant increase from 55.2% noted in the original audit (p=<0.001). Correct insulin administration in relation to meals was observed to be more in accordance with the local guideline in the re-audit compared to the original audit (71.2% *vs* 31.0% respectively, p=<0.001). A poor compliance to our local protocol with regards to the administration of supplementary Actrapid® (where prescribed) in relation to meals and when BGM was more than 8mmol/L was noted in both audits. However, when given, a significant improvement in the documentation of the timing and the dose administered was observed in the re-audit (p=<0.001*)*. Moreover, it was more often signed for compared to the first audit (Table 3).

Insulin Omission and Complications

Insulin was inappropriately omitted more often in the re-audit (3.8% to 10%, p = 0.044). No documented reason for insulin omission was present in all cases during the first audit and in 46.7% of cases in the re-audit. Inappropriate omission after treated hypoglycaemia or in the presence of normal but lowish BGM (between 4 and 5mmol/L) was present in 53.3% of cases in the second audit.

A greater number of complications secondary to errors in insulin prescription/administration were recorded in the re-audit (3.8% 2013 compared to 38.6% in 2017, p=<0.001). Observed complications are shown in figure 2.

Table 2: *Absolute numbers and percentage values of insulin prescription errors in the 1st audit and in the re-audit*

Insulin prescription errors		***1st Audit***		***Re-audit***		***P*** [a]
		N	***No (%)***	***N***	***No (%)***	
Written correctly		105	100 (95.2%)	150	134 (89.3%)	0.071
Insulin name legible		105	96 (91.4%)	150	138 (92.0%)	0.871
Doses legible		**105**	**86 (81.9%)**	**150**	**138 (92.0%)**	**0.021**
'Units' Written in full		**105**	**25 (23.8%)**	**150**	**62 (41.3%)**	**0.002**
When 'Units' not written in full	'U' written like a zero	80	2 (2.5%)	88	4 (4.6%)	0.469
	'Units' not written at all	80	5 (6.3%)	88	11 (12.5%)	0.160
Insulin prescribed in relation to meals		105	10 (9.5%)	150	11 (7.3%)	0.539
Supplementary Actrapid® prescribed*		**103**	**77 (74.8%)**	**145**	**124 (85.5%)**	**0.038**
Supplementary Actrapid® prescribed in relation to meals (when prescribed)		77	9 (11.7%)	124	9 (7.3%)	0.307
Supplementary Actrapid® algorithm present in file*		103	59 (57.3%)	145	99 (68.3%)	0.077
Correctly filled supplementary Actrapid® algorithm (if present in file)		59	38 (64.4%)	99	69 (69.7%)	0.495

[a] z-test

[*] *Patients on Novorapid® excluded*

No – absolute numbers

Table 3: *BGM and administration of insulin in 1st audit and re-audit*

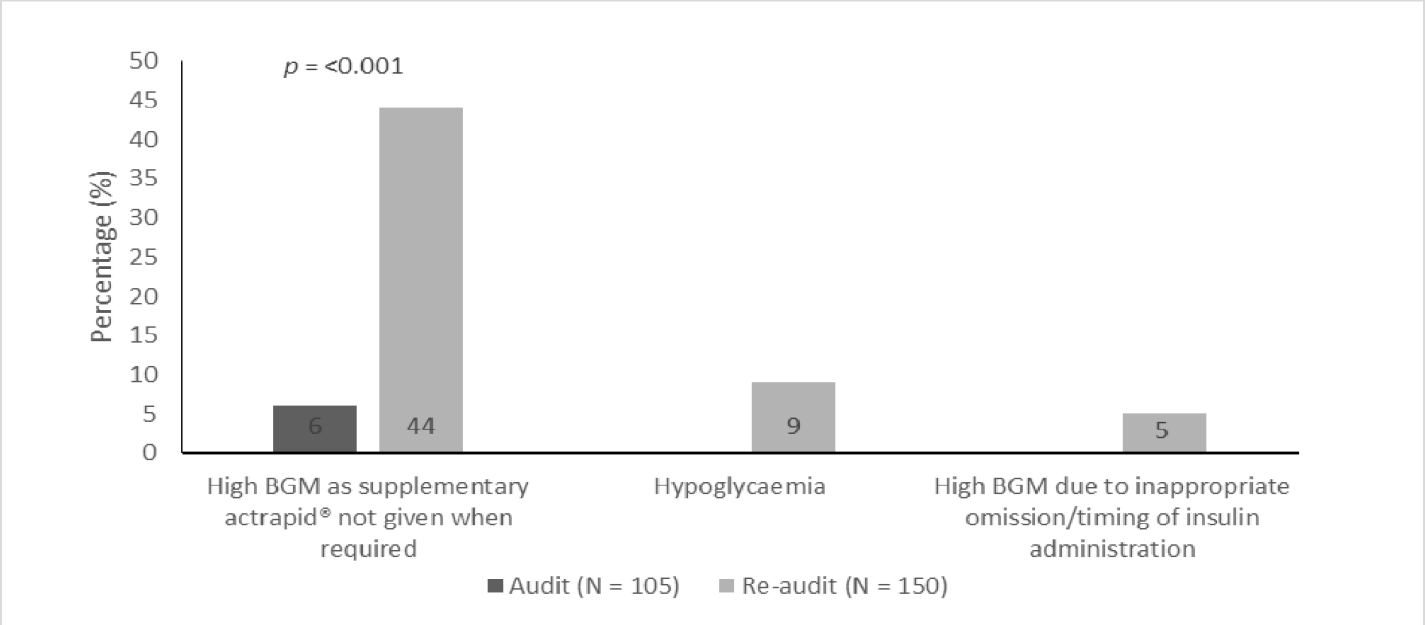
BGM and insulin administration	***1st Audit***		***Re-audit***		***P*** [a]
	N	***No (%)***	***N***	***No (%)***	
BGM monitoring	105	105 (100%)	150	149 (99.3%)	0.316
Correct time of BGM monitoring	**105**	**41 (39.1%)**	**150**	**92 (61.3%)**	**<0.001**
Less frequent BGM monitoring than recommended	64	5 (7.8%)	58	7 (12.1%)	0.434
More frequent BGM monitoring than recommended	**64**	**18 (28.1%)**	**58**	**39 (67.2%)**	**<0.001**
Administration of regular insulin signed on treatment chart	105	100 (95.2%)	150	142 (94.7%)	0.837
Time of administration of fixed dose charted	**105**	**58 (55.2%)**	**150**	**146 (97.3%)**	**<0.001**
Correct administration of insulin in relation to meals	**58**	**18 (31.0%)**	**146**	**104 (71.2%)**	**<0.001**
Supplementary Actrapid® administered as per algorithm*	97	26 (26.8%)	103	30 (29.1%)	0.714
Administered supplementary Actrapid® signed and dose given documented*	**97**	**54 (55.7%)**	**84**	**73 (86.9%)**	**<0.001**
Time of administered supplementary Actrapid® documented*	**97**	**52 (53.6%)**	**84**	**75 (89.3%)**	**<0.001**

[a] z-test

No – absolute numbers; BGM- blood glucose monitoring

**Where supplementary Actrapid® was prescribed and/or given; patients on Novorapid® excluded.*

Figure 2: *Type and frequency of complications secondary to errors in insulin prescription/administration*



BGM- blood glucose monitoring

Discussion

Educational sessions to doctors were effective in improving some aspects of insulin prescription, as prescribed insulin doses were more legible, insulin 'Units' were more frequently written in full, while supplementary Actrapid® was prescribed more often in patients not taking short-acting insulin analogues. Although, no improvement was noted with regards to writing insulin names correctly and legibly, this was done appropriately in the majority of cases. Educational sessions to nurses also led to a significant improvement in the timing of BGM and insulin administration in relation to meals and in the documentation of the time of any administered insulin.

Although more complications were documented in the re-audit, it is possible that blood glucose charts were scrutinized more closely in the re-audit, as data collection was carried out mainly by diabetologists/diabetes trainees, while in the first audit data collection was primarily carried out by foundation doctors and basic specialist trainees. The majority of complications occurred secondary to non-adherence with our local supplementary Actrapid® algorithm, resulting in persistently high BGM as supplementary Actrapid® was not always given when blood glucose was more than 8mmol/L pre-meals and at bedtime.

Unfortunately, no improvement was observed in the prescription of insulin including supplementary Actrapid® at the correct time in relation to meals despite the introduction of a new treatment chart, which included extra space dedicated for the documentation of any important instructions regarding the prescribed drug. This could be due to the heavy work-load doctors have to endure during duty hours. In order to ensure accurate prescription of insulin, including clear instructions of when to administer insulin and supplementary Actrapid® in relation to meals, we propose the drafting of a prescription chart devoted for insulin therapy, incorporating a blood glucose and ketone monitoring chart. The appropriate time when to check blood glucose in relation to meals will be written clearly on the treatment chart and will provide a space to prescribe hypoglycaemia medications. The treatment chart will also include a space to provide clear instructions with regards to the timing of insulin administration. Such treatment chart, including hypo- and hyperglycaemia trouble-shooting guidelines, was found to significantly improve compliance with evidence-based practice, insulin administration timing, hypoglycaemia control and provided a means to educate non-specialist staff.[14]

Inappropriate omission of fixed insulin doses was observed more often in the re-audit, with the majority of cases being due to a blood glucose of between 4-5mmol/L or hypoglycaemia. Further educational sessions to both nurses and doctors will be required to stress the importance of not omitting insulin in cases of hypoglycaemia. In such cases insulin doses should be reviewed, as insulin omission can result in rebound hyperglycaemia and diabetic ketoacidosis.[12]

Patients who are experienced and competent to manage their diabetes should be involved in decisions regarding their diabetes management.[4] Giving such patients the choice to self-monitor and self-manage their own diabetes and insulin may result in reduction of errors involving insulin administration including type and dose as well as timing in relation to meals, all of which can lead to better glucose control and reduced hospital stays. Therefore, implementing a policy for diabetes self-management at Mater Dei hospital, while allowing flexibility for changing clinical situations, may further help with reduction of insulin prescription and administration errors and resultant patient harm. The diabetes specialist team should be immediately involved if further education on diabetes self-management is required or if blood glucose is uncontrolled.[15]

Another strategy which was found to be successful, is the implementation of a multifaceted multidisciplinary prevention team, which would monitor insulin prescription, dispensing and administration. This strategy also involved authentication of any short-acting insulin orders above 25 units and other insulins above 50 units by different individuals, together with continued staff education on product-labelling warnings and on the importance to adhere to protocols.[16] In another study, the use of a diabetes specialist nurse prescriber, who reviewed prescription of insulin and oral hypoglycaemic agents (OHA), provided education to patients, medical and nursing staff when needed, continued to review insulin and OHA regimes and prescribed if medical staff were unavailable in emergency situations or if delay in prescribing will harm the patient, significantly reduced the number of insulin and OHA medication errors and reduced hospital stay.[17] Both aforementioned strategies may therefore help to re-enforce adherence to current local supplementary Actrapid® algorithm, so that supplementary Actrapid® can be administered when needed and at the correct time, thus avoiding both hypo- and hyperglycaemia. Computer-based clinical decision support systems might similarly help to further improve inpatient diabetes care.[18]

The results of our audit could have been constrained by three major limitations. Although we asked nursing staff in each ward the times when the main meals were distributed to patients, we could never know for sure whether the recruited patients ate their meals or had their food distributed at that exact time. Therefore, matching the documented time of any administered insulin with meal times might have been inaccurate. Moreover, any incorrect documentation of the time when blood glucose was monitored or when insulin was administered would have impacted our results. Lastly, there was no way of knowing for sure whether the correct type and dose of insulin was administered. Such limitations may be overcome by carrying out a prospective study, where insulin administration and its timing in relation to meals will be directly observed by the researcher.

In conclusion, although educational sessions led to some improvement in insulin prescription and administration, further work needs to be done to ensure patient safety in hospital and to avoid inadvertent patient harm secondary to errors in insulin prescription and administration.

Summary Box

What is known:

1. Insulin is a high-alert medication with a narrow therapeutic index.
2. Incorrect insulin prescription and administration can result in patient harm and medication error related mortality.
3. Errors in insulin prescription and administration can be the result of impaired communication, illegible handwriting, heavy work-loads and unawareness of the possible complications related to incorrect insulin prescription and administration.

New findings:

1. Education is effective in improving some aspects of insulin prescription and administration.
2. Lack of adherence to our local supplementary Actrapid® algorithm and inappropriate insulin omission resulted in capillary blood glucose readings to remain persistently high and in

rebound hyperglycaemia respectively.

3. The introduction of a new treatment chart with space dedicated for documentation of any important instructions related to the prescribed drug did not improve insulin prescription in relation to meals.

Acknowledgments

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References:

1. Institute for Safe Medication Practices. High-Alert Medications in Acute Care Settings. 2014. Available from: https://www.ismp.org/Tools/institutionalhighAlert.as.
2. Lamont T, Cousins D, Hillson R, Bischler A, Terblanche M. Safer administration of insulin: summary of a safety report from the National Patient Safety Agency. Bmj 2010;341:c5269.
3. Cousins D, Rosario C, Scarpello J. Insulin, hospitals and harm: a review of patient safety incidents reported to the National Patient Safety Agency. Clin Med (Lond) 2011;11(1):28-30.
4. Prescrire Editorial Staff. Insulin use: preventable errors. Prescrire Int 2014;23(145):14-7.
5. Hellman R. A systems approach to reducing errors in insulin therapy in the inpatient setting. Endocr Pract 2004;10 Suppl 2:100-8.
6. Department of Medicine - Diabetes Service. Supplemental insulin guideline for patients on oral intake. CPG Co-ordinating Committee Mater Dei Hospital; 2010.
7. Actrapid 100 international units/ml, Solution for Injection in a vial - Summary of Product Characteristics (SmPC) - (eMC). 2002. Available from: https://www.medicines.org.uk/emc/product/3849/smpc.
8. NovoRapid Penfill 100 units/ml - Summary of Product Characteristics (SmPC) - (eMC). 1999. Available from: https://www.medicines.org.uk/emc/product/4779/smpc.
9. Insulatard 100 international units/ml - Summary of Product Characteristics (SmPC) - (eMC). 2002. Available from: https://www.medicines.org.uk/emc/product/3848/smpc.
10. Lantus 100 units/ml solution for injection in a cartridge - Summary of Product Characteristics (SmPC) - (eMC). 2000. Available from: https://www.medicines.org.uk/emc/product/2376/smpc.
11. European Medicines Agency - Find medicine - Mixtard. 2008. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000428/human_med_000906.jsp&mid=WC0b01ac058001d124.
12. Joint British Diabetes Societies (JBDS) for Inpatient Care group. The Hospital Management of Hypoglycaemia in Adults with Diabetes Mellitus 3rd edition. Updated February 2018. Available from: http://www.diabetologists-abcd.org.uk/JBDS/JBDS_HypoGuideline_FINAL_280218.pdf.
13. 14. Diabetes Care in the Hospital: Standards of Medical Care in Diabetes-2018. Diabetes Care 2018;41(Suppl 1):S144-s51.
14. Rushmer R, Voigt D. MEASURE IT, IMPROVE IT: the Safer Patients Initiative and quality improvement in subcutaneous insulin therapy for hospital in-patients. Diabet Med 2008;25(8):960-7.
15. Joint British Diabetes Societies (JBDS) for Inpatient Care group. Self-management of diabetes in hospital [updated March 2012. Available from: http://www.diabetologists-abcd.org.uk/JBDS/JBDS_IP_SelfManagement.pdf.
16. Dooley MJ, Wiseman M, McRae A, et al. Reducing potentially fatal errors associated with high doses of insulin: a successful multifaceted multidisciplinary prevention strategy. BMJ Qual Saf 2011;20(7):637-44.
17. Carey N, Courtenay M, James J, Hills M, Roland J. An evaluation of a Diabetes Specialist Nurse prescriber on the system of delivering medicines to patients with diabetes. J Clin Nurs 2008;17(12):1635-44.
18. Nirantharakumar K, Chen YF, Marshall T, Webber J, Coleman JJ. Clinical decision support systems in the care of inpatients with diabetes in non-critical care setting: systematic review. Diabet Med 2012;29(6):698-708.

Original Article

Decisional Impulsivity in Obesity

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Abstract

Introduction: Elevations in impulsivity have been clearly shown in various psychiatric conditions, especially in those of addiction. Evidence does suggest some overlap between the pathological use of food and drugs but no clear evidence to date has been made available with regards to obesity. In this study we hypothesize that obese subjects would have relatively more impulsive profiles when compared to healthy volunteers.

Method: Delayed discounting is also studied by means of the Monetary Choice Questionnaire, also hypothesizing impairments in this subtype of impulsivity.

Results: Obese subjects sought less evidence prior to making a decision when compared to healthy controls. Greater delayed discounting was also evident in this cohort of subjects as compared to healthy ones. Premature responding was not shown to occur in the obese subjects.

Conclusion: Obesity is therefore characterized by impaired reflection impulsivity and greater delayed discounting. Both suggest a deficit in deciding on the basis of future outcomes that are more difficult to represent. This evidence could suggest possible therapeutic domains which need targeted interventions on the aspects of decision making deficits.

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Key words

Impulsivity, Obesity, Addiction

Introduction

Obesity is a major international public health issue. The mechanism underlying obesity is complex and heterogenous, including, but not limited to, metabolic, genetic, inflammatory and neurocognitive contributions. The question of self-control, or the ability to control our impulses is highly relevant to pathological eating behaviours. Impulsivity is a heterogeneous construct with discrete but overlapping neural substrates.[1] Impulsivity can be divided into decisional and motor subtypes. Decisional impulsivity is further divided into reflection impulsivity (the amount of information gathered before taking a decision) and delay discounting (a measure of subjective discounting of a delayed reward). Motor impulsivity divides into motor response inhibition and premature or anticipatory responding.[2]

Here we focus on assessing impulsivity in an adult population in Malta, a country highlighted as having one of the most obese populations

worldwide. In the 2009 Eurostat statistics, among the 19 European Union Member States for which data are available, the proportion of obese people in the adult population varied in 2008/9 between 8.0% (Romania) and 23.9% (UK) for women and between 7.6% (Romania) and 24.7% (Malta) for men.[3]

Converging studies have linked obesity with impaired delay discounting. Overweight and obese participants exhibited higher temporal discounting rates than underweight and healthy weight participants. A higher body mass index (BMI) was also strongly correlated with greater delay discounting.[4] Delay discounting is also correlated with clinical severity of BMI and depression, with greater discounting related to both disorders specifically for choices of comfort foods (i.e., the dessert and fried food).[5] Moreover, a higher discount rate is also predictive of higher calorie intake in obese women and children, and poorer treatment outcomes with less weight loss following intervention. Changing this concern with immediate reward into a more future-oriented outlook could therefore be useful in order to promote the choice of healthy foods and thereby facilitate a healthy weight. Behavioural interventions such as episodic future thinking rather than focusing on the immediate reward has been shown to reduce discount rates in obesity.[6]

In contrast, to delay discounting, only one study has investigated reflection impulsivity in obesity. Obese subjects with and without binge eating disorder (BED) were tested on the Information Sampling Task (CANTAB) with obese subjects without BED showing impairments in integration of available information in the cost condition.[7] Here we intend to use the Beads Task to test reflection impulsivity in obesity and has been shown to differ from the Information Sampling Task.[8] In the task, subjects sequentially view beads selected from jars with differing proportions of red and blue beads which has been shown to be associated with greater reflection impulsivity in substance use disorders, pathological gamblers[9] and binge drinkers.[8]

We have previously shown that neither obese subjects with or without BED were impaired in waiting impulsivity tested on the 4-Choice Serial Reaction Time task, whereas subjects with substance use disorders (abstinent alcohol and methamphetamine dependence, current cannabis and nicotine users, and binge drinkers) showed greater waiting impulsivity relative to healthy controls.[2] As this previous study assessed subjects with lower BMIs ; 34.68 and obese BED and 32.72 in Obese control, we sought to assess this measure in a group with higher BMIs. We hypothesized that obese subjects would have greater decisional impulsivity with higher delay discounting and greater reflection impulsivity relative to healthy controls.

Methods

Recruitment

Subjects with BMI of 30 or higher were recruited in Malta from an eating disorders unit ('Fondazzjoni Kenn Ghal Sahhtek'). Obese subjects were also screened for BED using the DSM-V criteria for BED. Age- and gender-matched healthy volunteers with a BMI of 26 or less were recruited via local advertisement.

The inclusion criteria included subjects who were either male or female English speakers, aged between 18-75 years. They also had to be deemed capable of giving a written informed consent. The exclusion criteria included, subjects with a history of severe neurological deficit or head injury. A clinical diagnosis of a significant DSM Axis one mental disorder, (e.g. schizophrenia, bipolar disorder, substance dependence) was also excluded. Subjects with a current major depression of moderate severity were excluded.

The study was approved by both the Cambridge Research Ethics Committee and the Malta Health Ethics committee. Written informed consent was obtained from all participants and reimbursement was given for their participation.

Questionnaires and tasks

Subjects completed the Alcohol Use Disorders identification test (AUDIT)[10] and Beck Depression Inventory.[11] Trait impulsivity was measured by the UPPS-P Impulsive Behaviour Scale[12] and the Spielberger State and Trait Anxiety Inventory.[13] Impulsive choice was assessed using the Monetary Choice Questionnaire[14] and reflection impulsivity was assessed using the beads task. Premature responding or "waiting impulsivity" was investigated by the 4 choice serial reaction time task. The latter is a novel translation of the task, based on the rodent 5-choice serial reaction time task, testing premature responding in disorders of

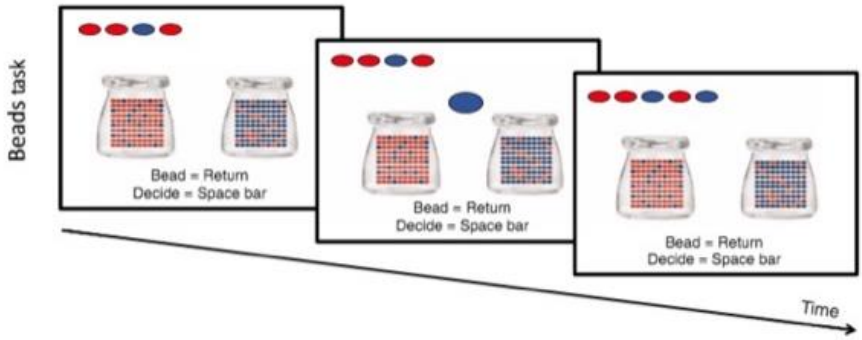
drug and natural food rewards.[2]

Beads task

Subjects were shown two jars on the computer screen with opposite ratios of red and blue beads (Jar 1: *P*=0.80 red; *P*=0.20 blue/Jar 2: *P*=0.80 blue; *P*=0.20 red) (Fig. 1). They were informed of the bead ratio and were told that beads from one of the jars would be presented one at a time in the centre of the screen. The subjects' goal was to infer whether the beads were drawn from Jar 1 or Jar 2. The subjects were free to view as many beads as they wanted to a maximum of 20 beads before committing to their decision. The decision was followed by a confidence rating in which subjects used a mouse to indicate the degree of confidence that their answer was correct, on a line anchored at 'Not confident' to 'Very confident'. Subjects were then informed that the next block would start. There was no feedback. The task was controlled for working memory by showing the coloured beads drawn across two rows at the top of the screen. There was no time limit to the task. The primary outcome measure was the number of beads drawn prior to a decision. There were three blocks of trials with the same bead order used in a previous study.[15]

Figure 1:

Beads task. Subjects viewed two jars with opposite ratios of red and blue beads (Jar 1: P=0.80 red; P=0.20 blue/Jar 2: P=0.80 blue; P=0.20 red). Beads selected from a single jar were sequentially shown to the participants. The goal was to infer from which jar the beads were being selected. After each bead was drawn, participants either chose to draw another bead or to make a decision. The drawn beads remained on display at the top of the screen. (Banca et al., 2015)



Delay discounting task

Delay discounting was measured using the Monetary Choice Questionnaire[14], composed of 27 items, in which participants choose between a small immediate reward and a larger delayed reward. The primary outcome measure was the discount parameter K.

Premature or Anticipatory Responding

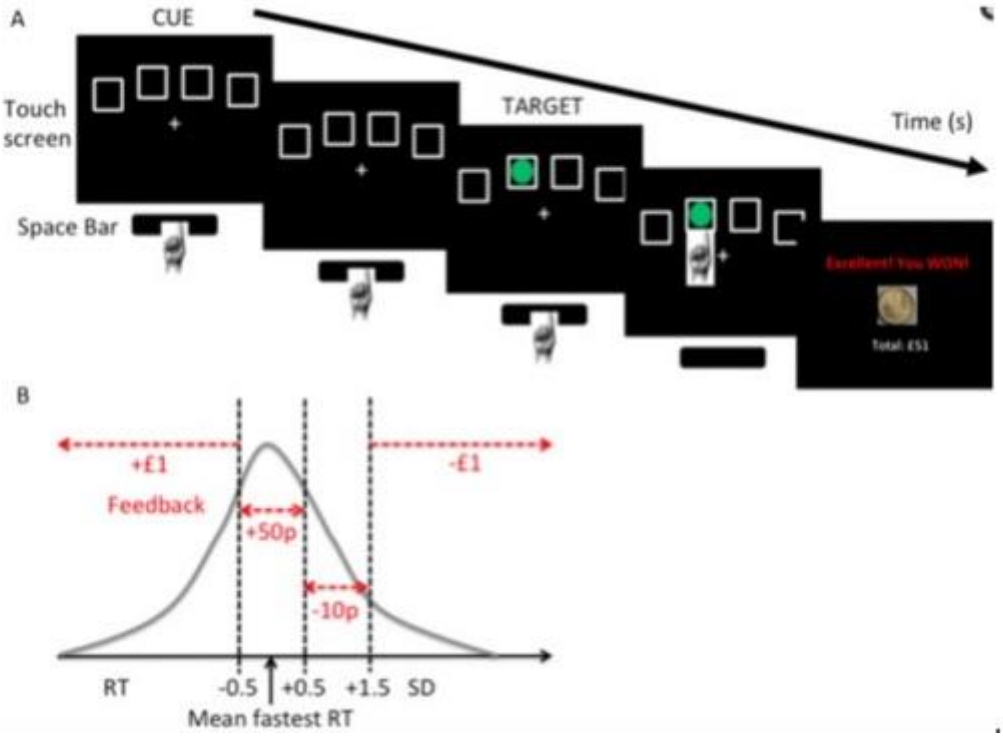
Subjects were seated in front of a touch screen (a Paceblade Tablet personal computer; Paceblade Technology, Amersfoort, the Netherlands). When four boxes appeared on the screen, the subject pressed and held down the space bar on the keyboard with their dominant index finger.

The space bar press indicated the "cue onset" time. After a specified period (cue-target interval), a green circle target appeared briefly and randomly in one of the four boxes. Subjects released the space bar and touched the box on the screen in which the target had appeared. The primary outcome measure was premature release of the space bar before target onset.

The block order was as follows: Baseline block 1; Test block 1; Baseline block 2; Test blocks 2–4. Baseline blocks without monetary feedback were used to individualize monetary feedback amounts for subsequent blocks on the basis of the mean fastest reaction time (RT) and SD of the individual. The four Test blocks with monetary feedback were optimized to increase premature responding and varied by duration and variability of the cue-target interval and the presence of distractors. *It was programmed in Visual Basic with Visual Studio 2005 and Microsoft .NET Framework 2.0 (Microsoft, Redmond, Washington) with the Euro currency for testing in Malta. Total task duration was 20 min.*[2]

***Figure 2**:*

Premature responding task. (A) Task. Subjects press and hold down the space bar when they see four empty boxes (Cue) on the touch screen. After a green circle (Target) appears in one of the boxes, the subject releases the space bar and touches the box in which the target had appeared. The main outcome measure, premature responding, is measured as release of the space bar before target onset. (B) Feedback for the Test blocks is individualized on the basis of the mean fastest reaction time (RT) and SD obtained in the Baseline block (Voon et al., 2014)



Statistical analysis of behavioral outcomes

The data were inspected for outliers (>3 SD from group mean) and for normality (Shapiro-Wilkes test $p>0.05$). As all the primary outcome measures were not normally distributed, they were analyzed using non-parametric independent samples Mann-Whitney U tests.

Results

Thirty obese subjects (age 36.46, SD=10.13) and 30 age- and gender-matched healthy volunteers (age 34.66, SD=9.39, t=.71, p=.47) were included in this study. Individuals with obesity had a mean BMI of 49.06 (SD=11.67) and HVs of 21.86 (SD=4.72, t=11.82, $p<.0001$). The male to female ratio was that of 8:22 for each group.

14 out of 30 obese subjects fulfilled criteria for BED. Compared to HVs, obese subjects reported significantly higher scores on depression (t=4.53, $p<.0001$), anxiety (t=3.49, $p=.001$), binge eating (t=6.08, $p=<.0001$) and impulsivity (t=3.06, $p=.003$). There were also statistically significant differences in binge eating disorder traits (t=6.08, $p=<.001$). However, no statically significant differences were notes with regards to drinking habits (t=-.74, $p=.46$) and obsessive compulsive disorder (t=1.78, $p=.07$).

Jumping to conclusions

Obese subjects required fewer beads prior to decision (greater impulsivity or lower evidence accumulation) ($p=0.047$) (Figure 3). There were no differences in the objective probability at the time of decision (Obese: 0.82 (SD 0.20); HV: 0.83 (SD 0.18), $p=0.641$) or in subjective confidence (Obese: 385.15 (SD 116.60); HV: 394.73 (SD 135.29), $p=0.605$).

Table 1: *shows the descriptive data and t-test differences for the obese and healthy subjects included in the study.*

	Obese (N=30)	HVs (N=30)	T test	P value
Age	36.46 (10.13)	34.66 (9.39)	.71	.47
Males:females	8:22	8:22		
BMI	49.06 (11.67)	21.86 (4.72)	11.82	<.0001
BDI	20.26 (11.47)	7.73 (9.88)	4.53	<.0001
SSAI	51.30 (13.21)	39.93 (11.93)	3.49	.001
BES	20.96 (10.48)	6.83 (7.21)	6.08	<.0001
AUDIT	3.50 (4.50)	4.33 (4.19)	-.74	.46
OCI-R	23.40 (11.37)	18.30 (10.70)	1.78	.07
UPPS total	137.93 (20.09)	121.65 (20.66)	3.06	.003

Figure 3*: Jumping to conclusions*
The graph shows the primary outcome measure, the number of beads viewed prior to decision in Obese subjects and matched healthy volunteers (HV)

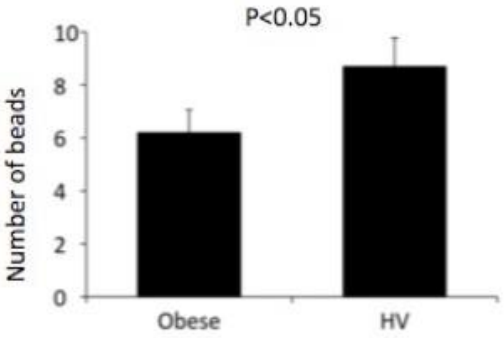
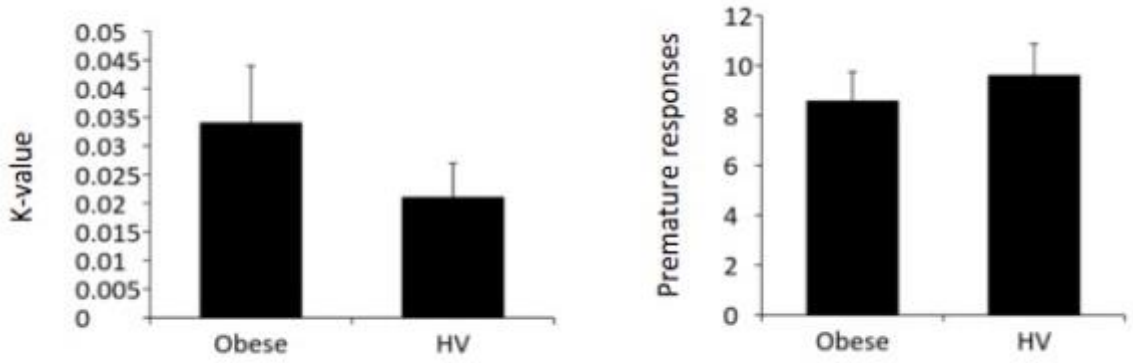


Figure 4: Delay discounting and premature responding
The left graph shows the primary outcomes of the delay discounting task and right shows the 4-Choice Serial Reaction Time task (4-CSRT).



Delay discounting

There was a trend towards greater discounting of delayed rewards or greater impulsivity in obese subjects compared to HV (Obese: 0.034 (SD 0.057); HV 0.021 (SD 0.034), p=0.054) (Figure 4). Data from 3 Obese subjects and 4 HV were removed as outliers (>3 SD from group mean).

Premature responding

There were no group differences between Obese subjects and HV in premature responding (Obese: 8.86 (SD 6.23); HV: 9.60 (SD 6.93), p=0.691) (Figure 4). Data from 2 Obese subjects were removed as outliers (>3 SD from group mean).

Discussion

We show that obese subjects relative to non-obese controls accumulate less evidence prior to decision making along with a trend towards enhanced delay discounting. No differences were observed between groups in waiting impulsivity. These findings emphasize impairments in decisional impulsivity and confirm previous findings of a lack of a difference in waiting impulsivity despite testing a population with higher BMIs in this current study[2]

In this study we show using the Beads task that obese subjects demonstrate a reduced tendency towards collecting salient information from the external environment before making a decision. In a previous study, obese subjects with or without BED tested using the Information Sampling Task (IST) did not show any differences in the amount of evidence sampled. Obese subjects without BED did show impaired integration of information to optimize outcomes over later trials within a cost condition.[7] The divergent findings between the two tasks highlight differences between the tasks or may reflect the higher BMI in the current group under study.

The IST and beads task test similar concepts. However, dissociation of results given by both tests may occur. A similar dissociation has been shown in studies in schizophrenia as subjects showed consistent impairment in the beads task while no differences between first episode psychosis patients and healthy volunteers were shown on the IST.[16] The disparity is likely to be a function of task differences. The IST presents information in a very explicit manner as it makes use of a 5x5 grid showing the total amount of information available to be sampled as a constant reminder. The latter may possibly act as an explicit external relative anchor and encouraging 'thinking ahead' of all possibilities, thus giving an overall representation of the task. In contrast, in the beads task subjects are not explicitly reminded that they can only choose 20 beads as this is only mentioned in the instruction phase. This makes the information less visually explicit. This makes it possible that individuals are less likely to always consider all options and thus may result in more impulsive decisions. Therefore, although the IST maybe more transparent and reduce uncertainty of the end point or total available information, the beads task maybe more ecologically valid as the total information available is not always explicitly known to the subject user.[8]

Secondly, in the beads task, bead sequences are generated from jars of known probabilities whereas in the IST, the generative probability distribution from which colored boxes are sampled is unknown. Thus, evidence is sampled from differing known probabilities. It may soon become apparent to participants that this generative probability is close to 50:50, pushing them towards caution. This may lead to subjects having an easier probability structure but more vague task structure which in return increases sensitivity to impulsive decisions. Thirdly, differences in monetary rewards are unlikely to explain different task results. In the fixed win condition, the IST is associated with winning points if correct while the beads task offers no explicit reward.[8]

In this study we find a trend supporting previous findings that obese subjects are more likely to choose the immediate, yet smaller reward.[4] Using the monetary choice questionnaire we show that obese subjects have a trend towards higher temporal discounting rates than healthy volunteers. Together this suggests the need to develop effective therapeutic interventions aimed at training individuals in the consideration of the future consequences.

We did not show differences in waiting impulsivity or premature responding in the obese subjects consistent with our previous study[2] suggesting that differences in BMI were unlikely to account for the lack of difference in this measure.

We show that decisional impulsivity is impaired in obesity. These two tasks might be

linked by impairments in the ability to link action with future outcomes in the face of uncertainty. These findings highlight a critical role for decisional impulsivity in obesity. Future work on the role of reflection impulsivity as a predictor for treatment outcome and as a target for therapeutic modulation are indicated.

Funding statement

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References

1. Voon V, Dalley JW. Translatable and Back-Translatable Measurement of Impulsivity and Compulsivity: Convergent and Divergent Processes. Current topics in behavioral neurosciences. 2016;28:53-91.
2. Voon V, Irvine MA, Derbyshire K, Worbe Y, Lange I, Abbott S, et al. Measuring "waiting" impulsivity in substance addictions and binge eating disorder in a novel analogue of rodent serial reaction time task. Biological psychiatry. 2014;75(2):148-55.
3. Eurostat. Aspects of daily living survey, 2009. In: Proportion of women who were overweight or obese onyH, editor. http://ec.europa.eu/eurostat/statistics-explained/index.php/Overweight_and_obesity_-_BMI_statistics: Eurostat; 2008. p. Figure one is the proportion of women who were overight or obese, 2008 and nearest year while figure 2 is the equivalent for males.
4. Jarmolowicz DP, Cherry JB, Reed DD, Bruce JM, Crespi JM, Lusk JL, et al. Robust relation between temporal discounting rates and body mass. Appetite. 2014;78:63-7.
5. Privitera GJ, McGrath HK, Windus BA, Doraiswamy PM. Eat now or later: self-control as an overlapping cognitive mechanism of depression and obesity. PloS one. 2015;10(3):e0123136.
6. Dassen FC, Jansen A, Nederkoorn C, Houben K. Focus on the future: Episodic future thinking reduces discount rate and snacking. Appetite. 2016;96:327-32.
7. Mole TB, Irvine MA, Worbe Y, Collins P, Mitchell SP, Bolton S, et al. Impulsivity in disorders of food and drug misuse. Psychological medicine. 2015;45(4):771-82.
8. Banca P, Lange I, Worbe Y, Howell NA, Irvine M, Harrison NA, et al. Reflection impulsivity in binge drinking: behavioural and volumetric correlates. Addiction biology. 2015.
9. Djamshidian A, O'Sullivan SS, Sanotsky Y, Sharman S, Matviyenko Y, Foltynie T, et al. Decision making, impulsivity, and addictions: do Parkinson's disease patients jump to conclusions? Movement disorders : official journal of the Movement Disorder Society. 2012;27(9):1137-45.
10. Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. Addiction (Abingdon, England). 1993;88(6):791-804.
11. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Archives of general psychiatry. 1961;4:561-71.
12. Whiteside SP, Lynam, D.R. The Five Factor Model and Impulsivity : using a structural model of personality to understand impulsivity. Personality and Individual Differences. 2001;30(4):669-89.
13. Spielberger CD. State-Trait Anxiety Inventory: Bibliography. 2nd ed. Palo Alto, CA.: Consulting Psychologists Press; 1989.
14. Kirby KN, Marakovic NN. Delay-discounting probabilistic rewards: Rates decrease as amounts increase. Psychonomic bulletin & review. 1996;3(1):100-4.
15. Moutoussis M, Bentall RP, El-Deredy W, Dayan P. Bayesian modelling of Jumping-to-Conclusions bias in delusional patients. Cognitive neuropsychiatry. 2011;16(5):422-47.
16. Huddy VC, Clark L, Harrison I, Ron MA, Moutoussis M, Barnes TR, et al. Reflection impulsivity and response inhibition in first-episode psychosis: relationship to cannabis use. Psychological medicine. 2013;43(10):2097-107.

Gastroscopic Pancreatic Necrosectomy – reporting the first two cases performed at Mater Dei Hospital

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Neville Azzopardi, Jurgen Gerada, Jo Etienne Abela

Abstract

Infected pancreatic necrosis was conventionally treated with open surgical techniques, but this approach was associated with a very high morbidity and mortality. Over the past two decades minimally invasive techniques have proved to be both effective and safe.

We present two cases of walled-off pancreatic necrosis secondary to severe biliary acute pancreatitis. Both patients were males in the fifties suffering from organ failure related to their disease. Regular pancreatic computed tomographic scans (CT) demonstrated evolving walled-off pancreatic necrosis.

Pancreatic necrosectomy was performed safely and effectively with readily available ERCP and gastroscopic equipment, using EUS as a crucial adjunct for confirmation and localisation. This procedure should be considered as the treatment of choice for this condition which commonly causes organ failure.

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Key Words

Severe acute pancreatitis (SAP), minimally invasive techniques, walled-off pancreatic necrosis (WOPN), necrotising pancreatitis (NP), acute pancreatic necrosis (ANC), necrosectomy

Case Presentation

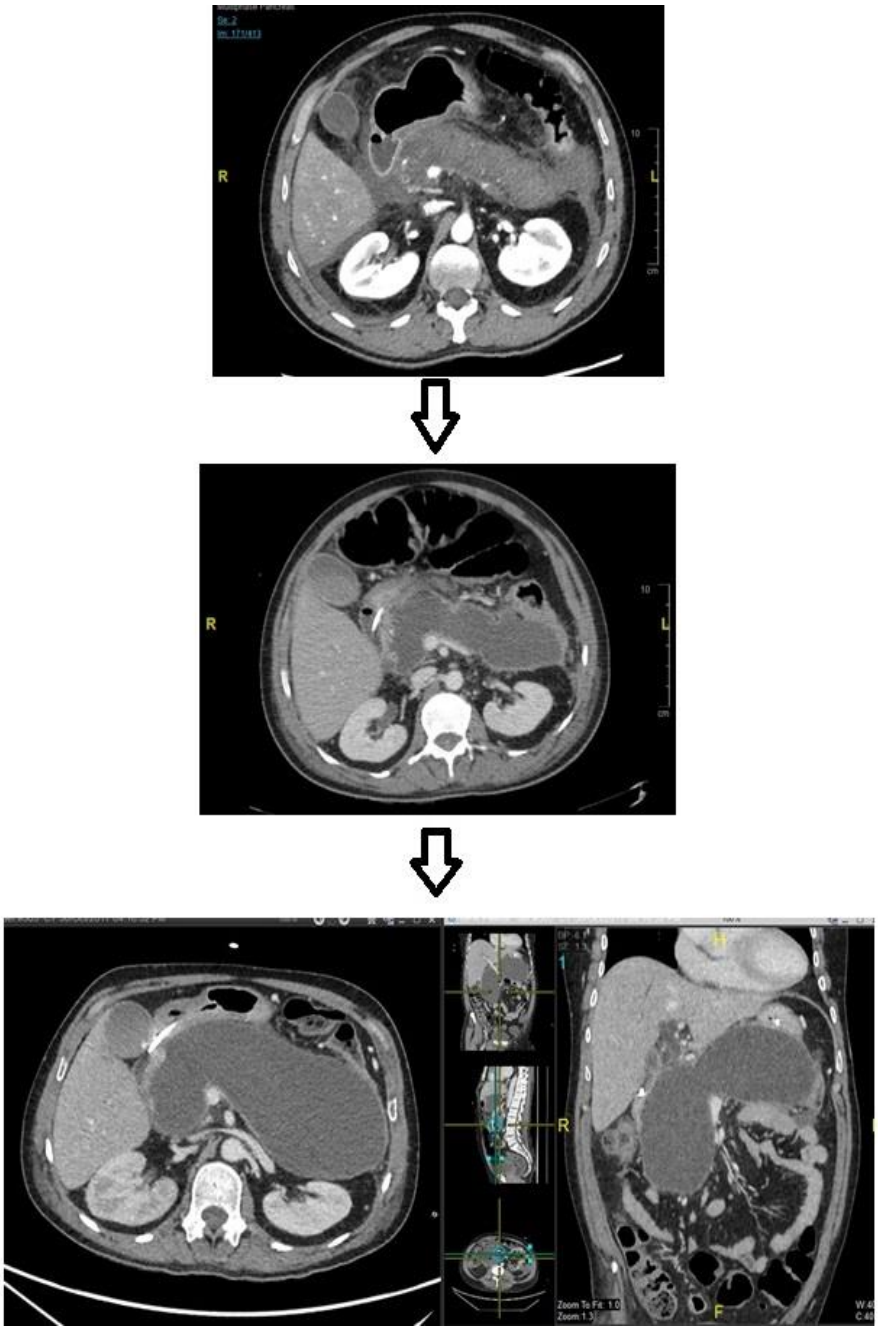
The two male patients in their fifties presented to the emergency department with severe, generalised abdominal pain associated with vomiting and pyrexia. Patient A was a previously fit and healthy individual with a normal body habitus. Patient B was a morbidly obese non-insulin dependent diabetic gentleman with a history of sleep apnoea and depression. Their admission serum levels were more than 2000U/l. Liver function tests were deranged with a cholestatic picture. CT confirmed the diagnosis of severe necrotising acute pancreatitis in both patients, with ultrasound scan confirming gall bladder stones. The patients were admitted for

supplemental oxygen, intravenous fluids and analgesia.

Two days post-admission, with a serum lactate level of 6.2mmol/L and a C-reactive protein of 442mh/L, patient A was transferred to the intensive care unit with multi-organ failure. He was suffering from hypoxia, hypotension, uncontrolled hyperglycaemia and renal failure. Total parenteral nutrition was instituted as there was failure of naso-gastric and naso-jejunal feeding.

Repeat serial CT scans performed during his 6 weeks of ITU admission confirmed that the pancreatitis was necrotising in nature with no enhancing parenchyma and revealed an evolving WOPN. *(Figure 1).*

***Figure 1**: Serial CT scans of patient A, showing progression of SAP to a large, sausage-like WOPN, measuring 19cm by 8cm in size, effacing the splenic vein*

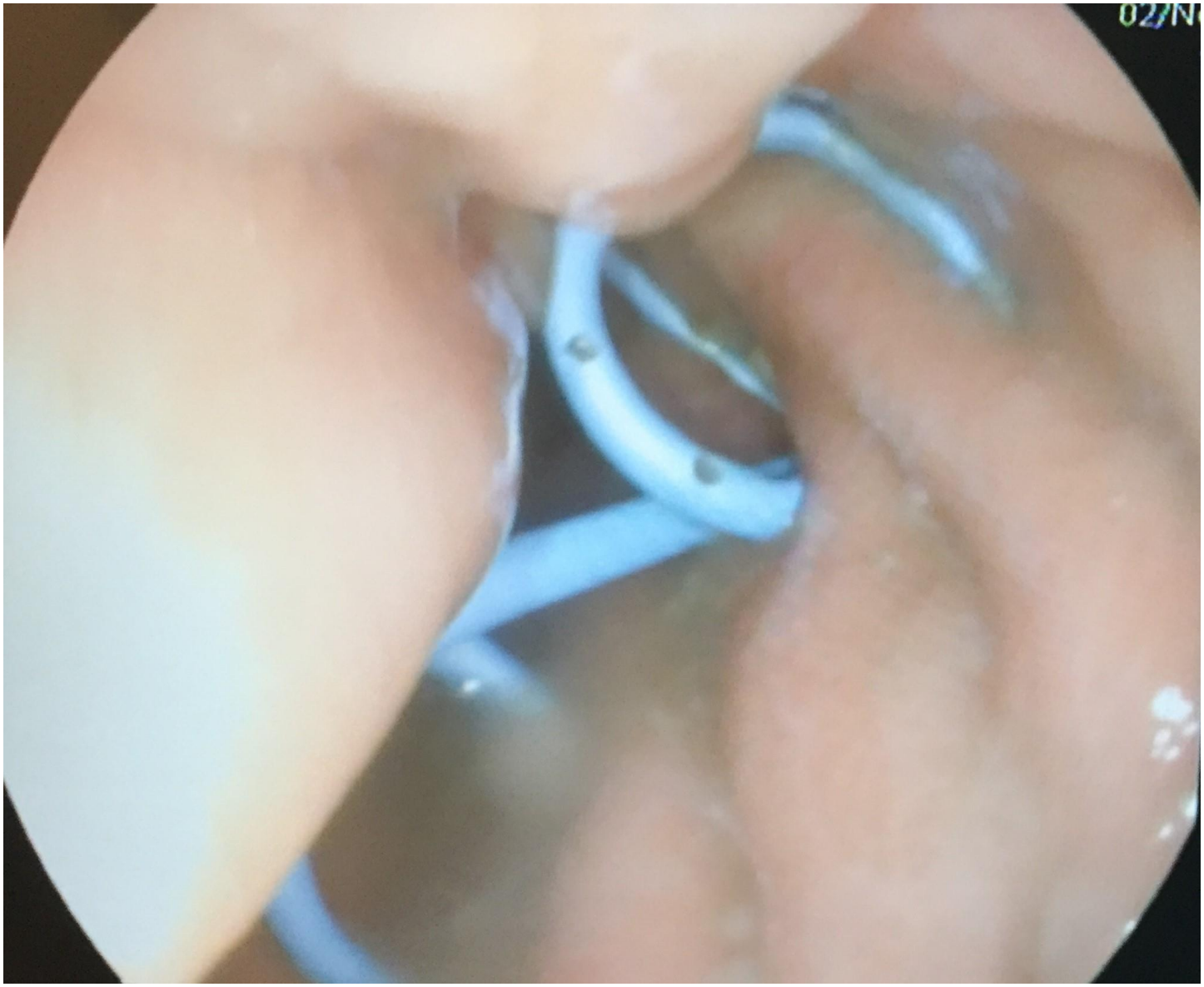


At 6 weeks, despite making a remarkable recovery in terms of his ventilatory and cardiovascular status, his septic markers deteriorated rapidly indicating the need for intervention.

Patient B had a more benign course and did not require intensive support until the 4th week post-admission. At this time his 20cm diameter WOPN caused gastric outlet obstruction, worsening jaundice with a bilirubin level peaking at 250mg/l, hypoxia, hypotension and renal failure. An intervention was performed at this time.

The procedures were performed under general anaesthesia, with antibiotic cover. With a linear EUS probe, the WOPN was delineated, punctured and a guide-wire passed into it. A side-viewing endoscope was passed, and the posterior gastric wall was punctured with a precut knife and the tip of a diathermy snare. A sphincterotome was then passed into the WOPN and the cyst-gastrostomy widened to 1cm. A forward viewing gastroscope was then exchanged and the cyst-gastrostomy was dilated to 20mm with an oesophageal balloon. The gastroscope was then inserted into the necrosis and debridement performed with biopsy forceps and a polyp-retrieval net. The cavity was washed out and pig-tail stents left in-situ *(Figures 2 and 3).*

***Figure 2**: Image taken during cyst gastrostomy and necrosectomy of patient A. Image show pig-tail stents in situ*



Both patients were observed in ITU for 48 hours. Their parameters improved steadily. Patient A developed insulin-dependent diabetes and was started on an insulin regimen. He required a further two necrosectomies and ERCP with stenting for biliary inflammatory stricture before his WOPN resolved *(Figure 4)* and an elective laparoscopic cholecystectomy and stent retrieval was then performed as definitive management. Patient B remained well and is due to have a cholecystectomy.

***Figure 3**: Patient A; Gastroscopic view of necrotic material issuing from cyst-gastrostomy alongside pig-tail stent*

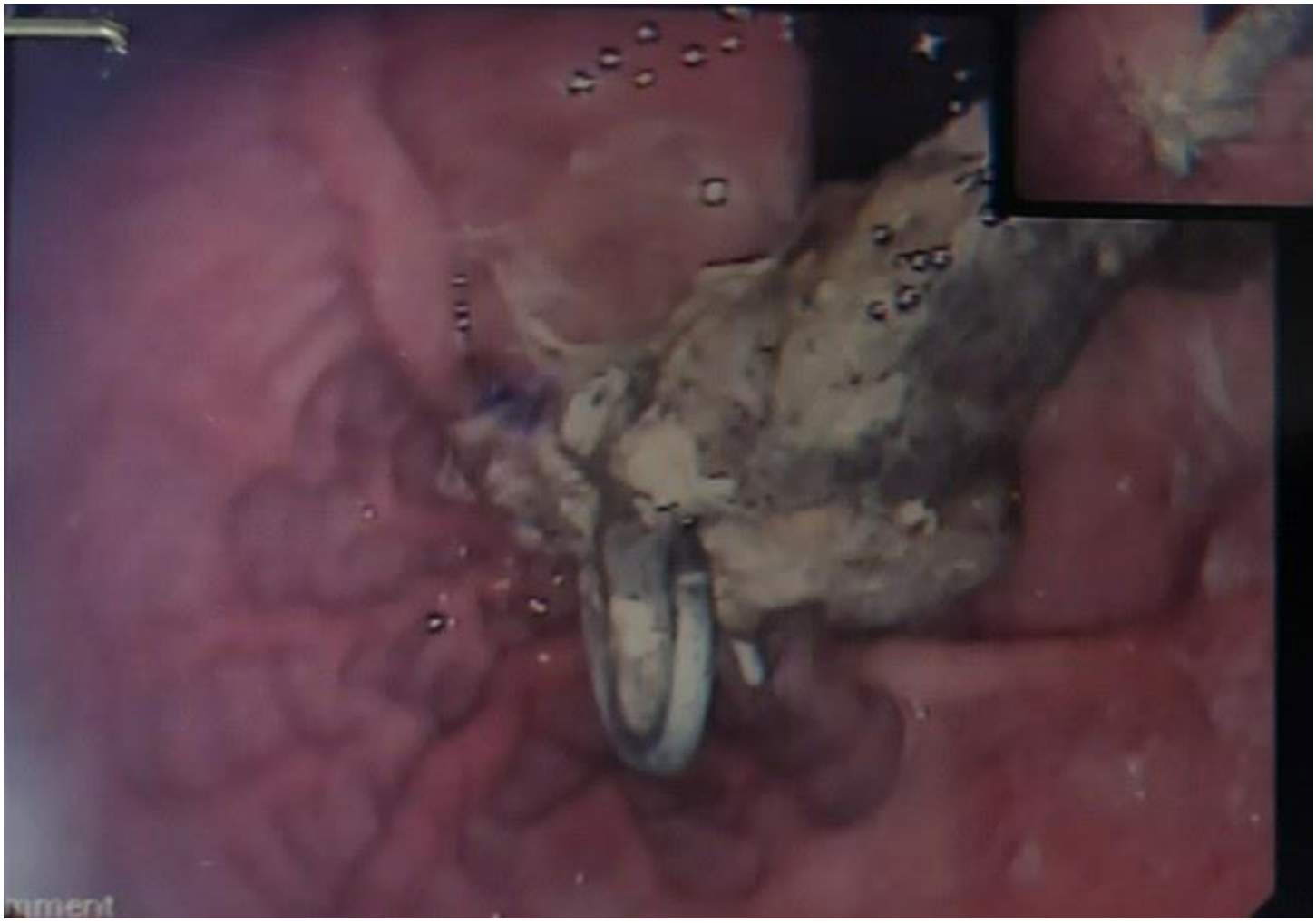
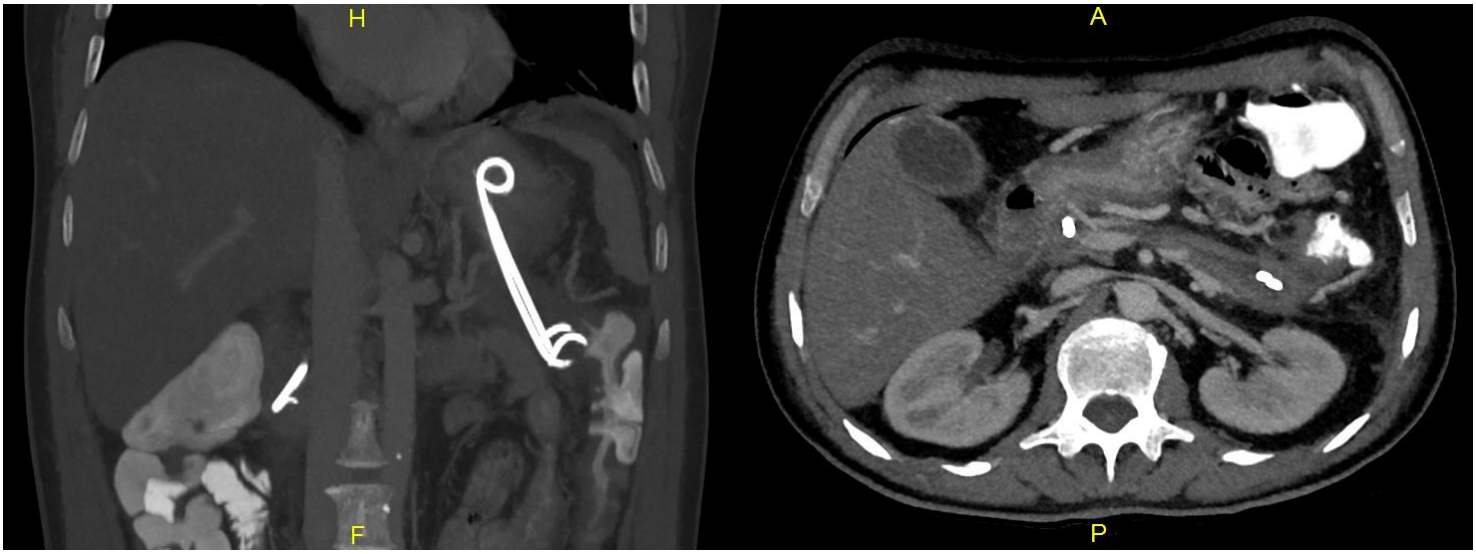


***Figure 4**: Patient A; CT images in coronal and axial views showing an ERCP stent in place, as well as the pig-tails in position between the stomach and a shrunken WOPN*



Discussion

Acute pancreatitis has a reported annual incidence of 13-45 cases per 100,000, making it one of the most common gastrointestinal disorders requiring acute hospitalisation[4]. The incidence is increasing globally and is a major burden on health care worldwide. Pancreatic fluid collections occur in about 10% of patients with acute pancreatitis[2].

Within the first 4 weeks of presentation, fluid and necrotic material may collect within the lesser sac and retroperitoneum creating an acute necrotic collection (ANC). WOPN develops after 4 weeks have elapsed from presentation of acute NP and the collection persists by becoming encapsulated *(Atlanta Classification, revised in 2012 and 2016).* WOPN can remain sterile but infection rapidly causes organ dysfunction. In the cases we present, the patients developed this complication in addition to causing gastric outlet obstruction and obstructive jaundice.

The International Association of Pancreatology and American Pancreatic Association (IAP and APA respectively) guidelines for the management of acute pancreatitis were published in 2013 and described indications for intervention in NP. These include; suspicion of, or documented, infected pancreatic necrosis with clinical deterioration, gastric outlet obstruction, biliary obstruction, organ failure, persistent pain and disconnected duct syndrome. Intervention in infected NP is generally delayed until it has become WOPN.[4]

Conventionally, techniques including open necrosectomy were performed for WOPN and other pancreatic collections. However, in the past two decades, there has been a move towards minimally invasive techniques and step-up techniques. Step up techniques involve first the drainage of the collection, followed by necrosectomy. Minimally invasive techniques involve percutaneous (retroperitoneal or transabdominal) or endoscopic approaches.[5,7]

In the case of endoscopic interventions, an endoscopic ultrasound or conventional endoscope is used and a cystgastrostomy tract is formed and dilated with large diameter (10–20 mm) balloon. Multiple double-pigtails stents or metallic biliary stents are then inserted, allowing drainage into the gastrointestinal tract. This is generally followed by entering the collection using a forward viewing endoscope, performing a washout of the WOPN cavity with saline or/and hydrogen peroxide and followed by a necrosectomy using endoscopic equipment such as large forceps, baskets, Roth nets and balloons.[1,6,7]

There have been various studies carried out showing the benefits of endoscopic techniques as

compared to open surgical techniques. A few benefits include decreased new onset diabetes, decreased pancreatic fistula formation, decreased pro-inflammatory response, and essentially, decreased morbidity and mortality.[5]

Pancreatic necrosectomy can be performed safely and effectively with readily available ERCP and gastroscopic equipment, under EUS localisation. This procedure should be considered as treatment of choice for patients developing WOPN.

List of Abbreviations

A&E	Accident and Emergency
ANC	Acute necrotic collection
CT	Computed tomography
ERCP	Endoscopic retrograde cholangio-pancreatography
ITU	Intensive therapy unit
NP	Necrotising pancreatitis
NIV	Non-invasive ventilation
SAP	Severe acute pancreatitis
TPN	Total parenteral nutrition
WOPN	Walled-off pancreatic necrosis

References

1. Abela JE and Carter CR. Acute pancreatitis -a review. *Surgery (Oxford)* 2010;**28** (5):205-211
2. Banks PA, Bollen TL, Dervenis C et-al. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus. *Gut* 2012;**62** (1): 102-11
3. Bryan R. Foster, Kyle K. Jensen, Gene Bakis, Akram M. Shaaban, Fergus V. Coakley. Revised Atlanta Classification for Acute Pancreatitis: A Pictorial Essay. *RadioGraphics* 2016;**36** (3):675-87
4. Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. *Pancreatology* 2013;**13**(4 Suppl 2):e1–15
5. Bakker O.J., van Santvoort H.C., van Brunschot S. et al. Endoscopic transgastric vs surgical necrosectomy for infected necrotizing pancreatitis: a randomized trial. *JAMA* 2012;**307**: 1053–1061
6. Trikudanathan G, Attam R, Arain MA, et al. Endoscopic interventions for necrotizing pancreatitis. *Am J Gastroenterol* 2014;**109**: 969–81.
7. van Santvoort HC, Besselink MG, Bakker OJ et al.; Dutch Pancreatitis Study Group. A step-up approach or open necrosectomy for necrotizing pancreatitis. *N. Engl. J. Med* 2010;**362**(16),1491–1502