TIMING OF COMPLICATIONS FOLLOWING ELECTIVE CRANIOTOMIES

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Declaration

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List of Abbreviations

APACHE	Acute Physiology and Chronic Health Evaluation
CI	Confidence Intervals
CRF	Case Report Form
ERAS	Enhanced Recovery After Surgery
GCS	Glasgow Coma Scale
GSH	Groote Schuur Hospital
HCU	High Care Unit
ICU	Intensive Care Unit
IQR	Interquartile Range
PONV	Post-Operative Nausea and Vomiting
RN	Registered Nurse
ROC	Receiver Operating Characteristics
SD	Standard Deviation
SOP	Standard Operating Procedures
TBI	Traumatic Brain Injury
UCT	University of Cape Town

Chapter 1: Literature Review

Introduction

Objectives

This literature review focuses on answering the following two questions:

1) What are the current international practice standards for immediate post-surgical care of elective craniotomies in adults?

2) What are the significant complications in the first 24 hours after elective craniotomy? Specifically, within what time frame do these complications occur?

Literature Review Search Strategy

A review of the literature was performed using Boolean logic with the two search engines: Pubmed and Google Scholar. The words and terms used were “craniotomy OR craniotomies OR neurosurgery”, “elective OR non-emergent”, “post-operative OR postoperative”, “critical care OR intensive care” and “complications”. Some for this audit.

Articles not published in English were excluded. Articles were restricted to an adult population.

Summary of the literature

Background

Routine post-operative admission of elective neurosurgical cases to intensive care units (ICUs) was first questioned in the 1980’s [(1)] and in the last decade there has been a slowly mounting body of evidence that has challenged this practice.[(2-4)] The reason it has been questioned is due to growing pressure to avoid excessive ICU costs and to use hospital resources effectively.[(5)] While effective utilization of resources in hospitals is a worldwide challenge, it is even more applicable in developing countries such as South Africa, where there is significant neurosurgical ICU bed pressure due to the added burden of a high number of patients suffering traumatic brain injury (TBI).

Tradition and general practice dictates that elective craniotomies be admitted postoperatively to higher care units (HCUs) or ICUs for at least 24 hours.[6] Our own institution, Groote Schuur Hospital (GSH), follows this protocol.

This practice is not evidence-based and in recent years has become a matter of debate.[5, 7, 8]

The reasonable argument for this conservative approach is that close monitoring leads to early detection and intervention of potentially devastating complications. The focus is specifically on neurological complication detection and prevention by strict monitoring and support of systemic and neurological function.[9]

The counter argument is that HCUs and ICUs resources should effectively be utilised, not only for monitoring purposes, but for monitoring that will lead to ICU level intervention.[1, 3] Evidence shows that the incidence of serious neurological complications requiring ICU level intervention is very low in post-elective craniotomies. Furthermore, the majority of these complications happen within the first few hours after surgery.[2, 10-12]

The reasons for the variety of postoperative approaches worldwide are multi-factorial and are unlikely to solely stem from traditional practice. The presence of specialised centres, with the availability of skilled surgeons with special interests in specific elective neurosurgical procedures along with the presence of well-resourced ICU (and even general) wards with appropriately trained staff, all contribute to deriving the protocols for each centre.

What follows in this narrative review is a summary of the current worldwide practice protocols for post-operative neurosurgical care as well as the significant complications that occur after elective neurosurgical cases and what the available evidence indicates about the timing of these complications.

Current worldwide practice for immediate post-surgical care of elective craniotomies in adults

The latest consensus summary on multimodality monitoring in neurocritical care was a collaboration between *The Neurocritical Care Society* and other international critical care societies. Many of the recommendations from this consensus were supported by low quality evidence and related mainly to acute or TBI monitoring.[13] The consensus does not indicate when significant post-operative complications will occur or give a timeline as to the need (if any) for routine postoperative ICU care in elective neurosurgical patients.

The rationale behind routine ICU admission is that avoidable complication rates following neurosurgical procedures of all types is high.[6] However, of these patients only a small proportion of patients undergoing elective craniotomy require high care interventions.[3] Despite this fact,

immediate post-surgical practice worldwide is varied, with some institutions taking a more conservative approach with a mandatory overnight stay, while others will only have patients being admitted to a post-surgical ICU if intracranial complications develop intra-operatively or immediately postoperatively.[6] Despite the poverty of high grade evidence in this field, less conservative post-operative standards in practice have been promising. Day-case craniotomies have been performed with high success rates in both Canada and the UK in recent years.[14, 15] Some institutions have been safely managing patients with their own risk stratification protocols, in selecting which patients will be discharged to the neurosurgical ward after elective craniotomies. All of the patients in these studies were observed for a period ranging from four to six hours in a post-operative anaesthetic HCU or high care recovery area before decision to discharge to the ward.[3, 4, 16] This has led to no significant difference in patient morbidity or mortality outcomes. In fact, one study showed a decreased length of hospital stay in the non-ICU group.[3]

This might be explained by the fact that patient's selected to go to ICU are usually more critically ill, and there is also the argument to be made that the inertia of starting off in an ICU, delayed mobilisation and less physiotherapy in the ICU setting will impact length of hospital stay.

A suggested approach would be to select for high risk patients for post-operative high care admission using validated scoring systems such as the APACHE (Acute Physiology and Chronic Health Evaluation) score. One study found diabetes and older age to be independent predictors of admission.[10] Another found that age was not an independent predictor of medical or neurological sequelae and that patients who undergo uncomplicated surgery and emerge from surgery without difficulty do not require ICU observation.[4] Whilst successful in pelvic and gastrointestinal surgery, enhanced recovery after surgery (ERAS) principles have been suggested for elective craniotomies.[14] Unfortunately, evidence is currently insufficient to generalise these principles to elective neurosurgery.

A recent cohort study conducted in the Netherlands by ter Laan et al. showed that by implementing a Standard operating procedure (SOP) whereby a multidisciplinary regimen involving the neurosurgeon, anaesthesiologist and nursing staff is undertaken in carefully selected patients, there is no need for uncomplicated cases to go to a high dependency unit postoperatively.[17] In fact, they showed that the cohort of patients enrolled in this SOP had a lower complication rate, duration of hospital stay and there was the added benefit of significant cost reduction. This regimen included intra and early postoperative agreement by both neurosurgeon and anaesthesiologist that the patient did not require ICU, a 1 hour monitored stay in recovery with specific easy to perform bedside neurological tests over and above routine monitoring and a 1 hour assessment by a neurosurgeon (or trainee neurosurgeon) to declare the patient fit for discharge to a neurosurgical ward.

Significant complications in the first 24 hours post elective craniotomy and the timing thereof

Post-operative complications following elective craniotomy are not uncommon. Lonjaret et al. demonstrated an incidence of complications ranging from 31% up to 45%, which included neurological, post-operative nausea and vomiting (PONV) as well as haemodynamic compromise.[12] However, some of these complications, while distressing for the patient, are generally self-limiting and have no effect on morbidity and mortality. PONV is an example of a minor complication.

The post-operative complications of major concern in elective craniotomies can be divided into neurological and systemic adverse events impacting on brain function (i.e. complications leading to poor oxygenation and perfusion of the recently operated brain).

Major adverse neurological events include: intracranial bleeds, cerebral oedema, ischaemic infarcts and seizures.[8] Specifically, intracranial haematoma and seizures require immediate higher care level intervention. The incidence of all cause neurological complications is in the region of 16%.[12]

Occurrence of a post-operative intracranial haematoma is associated with particularly high morbidity and mortality and is the complication that is most feared in the post-operative period. A landmark trial conducted in England by Taylor et al found the incidence of intracranial haematoma post-operatively ranges from 0.8% to 2%. Of note, this included both elective patients and patients with TBI. Importantly, almost 90% of the patients who developed a haematoma presented with new neurological deficit within 6 hours following surgery.[11]

The authors concluded that patients undergoing elective supratentorial neurosurgical procedures who regained pre-operative neurological function, could be safely discharged to a general ward after six hours. However, they also recommended that patients with prolonged surgery, marked blood loss or who underwent posterior fossa surgery warranted longer ICU stays. A smaller study found that the incidence of intracranial haematoma requiring surgical intervention was about 1%, and all of these patients presented within 2 hours of admission to an ICU.[8] They found that predictors of complications included failure to successfully extubate in the operating room and surgical time of more than 4 hours. A larger cohort study also found that 1% of patients developed a clinically significant haematoma post-operatively, but made no mention of the timing of symptoms to herald this complication.[10]

Post-operative seizures have a lower incidence than intracranial haematoma, close to 1%.[12] While having a seizure is a serious complication, its low incidence has deemed it less of a concern than development of a haematoma. There is no available data to predict timing of postoperative seizures.

Significant systemic adverse events include respiratory failure requiring ventilator support and hemodynamic instability requiring intravenous drug administration or infusions.
The need to provide medication to control blood pressure, either to decrease it with intravenous anti-hypertensives, or to increase it with vasopressors, is a common systemic complication encountered in postoperative neurosurgical patients. Management of blood pressure is important to maintain perfusion of the brain and prevent serious complications such as ischaemic stroke and intracerebral haemorrhage. A prospective cohort study found that 30% of patients required haemodynamic support in the ICU, with the need for the use of intravenous antihypertensives being the most common intervention required. The authors go on to state that if you remove the need for intravenous blood pressure support, only 8.25% of patients required ICU level care.[10] The timing of development of the need for haemodynamic support was not mentioned, but it was found that diabetics, patients with large intra-operative blood loss or need for transfusion and those that underwent prolonged surgery were more likely to require postoperative haemodynamic support. The need for ventilatory support is a rare complication in patients that were extubated in the operating room, with a low percentage (0.75%) requiring re-intubation in the ICU.

Conclusion

Evidence from developed countries suggests that patients undergoing uncomplicated elective supratentorial craniotomy with return to baseline neurological function six hours post-operatively can be safely discharged to a general ward as their risk of developing a significant neurosurgical complication thereafter is small.
Unfortunately, there have been no studies conducted in this specific field in the African or low-middle income context. The lower socio-economic environment, later pathology presentation, lack of medical compliance or access to primary health care and limited medical resources serves as a background that might influence post-operative complications uniquely. With the high TBI load in our setting competing for ICU and HCU beds, the need to investigate the incidence and timing of complications is valid as it will help to determine whether we can decrease the traditional postoperative length of ICU stay for elective neurosurgical cases. Should it be deemed safe practice in this setting, it will improve patient turnover and decrease ICU costs. Promotion of higher patient turnover without affecting patient outcomes negatively is the ultimate aim.

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Chapter 2: Manuscript

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Timing of complications following elective craniotomies:
a retrospective observational study.

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Abstract

Background : Conservative prolonged observation periods after elective craniotomies with admission to neurosurgical higher or intensive care units (ICU) have been the norm for many decades. This practice is neither evidence based nor a cost-effective use of medical resources. This observational audit aimed to establish the incidence and timing of serious complications after elective craniotomies in a low-middle income country context.

Methods: The medical records of adult patients who had elective craniotomies for the 2-year period of March 2016-February 2018 at Groote Schuur Hospital were reviewed. Complication incidence and timing was analysed in all patients admitted to either the neurosurgical high care unit (HCU) or ICU post-operatively for the initial 24hr period. The specific complications in our audit was defined as: a decrease in Glascow Coma Scale (GCS) of more than 2 points from the preoperative baseline score, new onset or worsening motor deficit, seizures, diabetes insipidus, haemodynamic instability, severe hypertension, tracheal intubation or noninvasive ventilatory support, and death. Statistical analysis was primarily descriptive.

Results: A total of 189 elective craniotomy patients were included in our audit for the 2-year period mentioned. In this study 37/189 (19.6%) patients developed 1 or more major complications during the initial 24 hr post-operative period. Of these 37 patients, 31 (83.8% [95% CI 71.9-95.7]) patients developed their first onset complication within six hours of admission to the HCU or ICU, and the remaining 6 (16.2% [95% CI 4.3-28.1]) in the subsequent 18 hours. All patients who developed life threatening complications (airway, ventilation or haemodynamic support) had their first onset complication (“red flag”) within six hrs of admission.

Conclusion: Our audit suggests that consideration should be given to discharge patients to a general neurosurgical ward after an uncomplicated six hour postoperative ICU stay. While a significant amount of first onset complications may occur if a patient is discharged to the neurosurgical ward

after this time period, these complications were unlikely to be immediately life threatening and should not require more than standard neurosurgical ward observations to detect.

Introduction

Finding the balance between cost-effective medical resource utilisation, and safe clinical practice is a challenge worldwide.[1] This is particularly important regarding high care units (HCUs) and intensive care units (ICUs), where costs are high and bed numbers limited.[2] In recent decades, the appearance of speciality driven HCUs and ICUs has become common in tertiary hospitals. In particular, the introduction of neurosurgical ICUs has been associated with improved morbidity and mortality, although the evidence has been more compelling for emergency neurosurgical procedures.[3, 4]

Serious complications requiring intervention after elective craniotomies are infrequent, but can be associated with devastating morbidity and mortality. Therefore, elective neurosurgery has been traditionally followed by a 24 hour period in a neurosurgical HCU or ICU.[5]

The recommended duration of higher level of observation after elective neurosurgery is not evidence based, and therefore not standardised across institutions. Due to the high impact of hospital costs and limited resources, elective postoperative neurosurgical admissions to HCUs or ICUs has been questioned and shorter monitoring periods have therefore been suggested in recent years.[6-9] Some studies have looked at risk-stratifying patients, while others have proposed enhanced recovery programmes after neurosurgery,[10-12] and some units have even explored the performance of day-case craniotomies.[13]

High-quality evidence is lacking for the safety of shorter monitoring periods in this setting. There is especially limited data on patients in low- and middle-income countries, where patients frequently present later with advanced and complicated pathology, and experience delayed surgery due to resource constraints. This could influence the timing and nature of postoperative complications. Due to the high caseload of trauma in South Africa which leads to considerable competition for HCU and ICU beds between elective neurosurgical cases and those with traumatic brain injury, it would be useful to ascertain whether we can safely discharge elective neurosurgical patients out of these units earlier than is traditionally accepted.

This observational audit aimed to establish the incidence and timing of significant complications after elective craniotomies in the South African context. We hypothesised that all clinically significant complications that require higher level monitoring or care will present in the first six

hours post-operatively, and thus a shorter postoperative HCU or ICU stay would not be associated with significant morbidity and mortality.

Methods

This retrospective audit analysed the intra-operative, and first 24 hours postoperative course, of all patients admitted to the neurosurgical HCU and ICU after elective craniotomies at Groote Schuur Hospital (GSH), Cape Town, South Africa, for the 2-year period: March 2016-February 2018. Ethics approval was obtained from the Human Research Ethics Committee of the University of Cape Town (HREC 857/2017). The requirement for informed consent was waived. All patients over 18 years of age requiring a non-emergent craniotomy for supra- or infratentorial neuropathology, and admitted postoperatively to the neurosurgical HCU or ICU, were included in this audit. Exclusion criteria were surgical neurosurgical procedures not meeting the definition of craniotomy (surgery that included two or less burr holes, endoscopic sinusoidal surgery, ventriculo-peritoneal shunt, external ventricular drain, and stereotactic neurosurgery) and patients who received postoperative mechanical ventilation for more than one hour, or in whom postoperative tracheal extubation was unsuccessful within one hour after admission.

The neurosurgical HCU and ICU at GSH each have six beds. The main difference being that the HCU offers no ventilatory support. The ICU has a registered nurse (RN) to patient ratio of 1:2, assisted by a staff nurse and training nurse, while the HCU has a RN to patient ratio of 1:3, similarly assisted.

The primary objective of this retrospective audit was to determine and compare the number of patients with complications presenting within the first six hour period of admission, to the number with a first onset of a complication presenting within the subsequent 18 hour period, of the traditional 24 hour admission to HCU or ICU after elective craniotomy. Complications were defined as significant if objective assessment was possible, and ICU or HCU management deemed necessary for either observation or treatment purposes. These complications specifically included a decrease in Glasgow Coma Scale (GCS) of more than two points from the preoperative baseline score, new onset or worsening motor deficit, seizures, diabetes insipidus, haemodynamic instability (requiring inotropic or vasopressor support), severe hypertension (requiring intravenous antihypertensive therapy), tracheal intubation or noninvasive ventilatory support, and death.

Of note, it is not standard practice to give seizure prophylaxis intra-operatively at GSH for elective craniotomies and intravenous antihypertensive therapy is instituted as per the discretion of the treating doctor in the HCU or ICU.

The secondary objective of this study was to analyse the incidence and identify possible risk factors for postoperative complications within the first 24 hours. Collection of demographic and perioperative information, regarding each patient was done. (Table 2)

Data collection

The UCT neurosurgical electronic database for the period of March 2016 to February 2018 was used to identify a list of charts for review. This list was subsequently correlated with the patient admission registers for the neurosurgical HCU and ICU for this period. All the relevant charts were collected from medical records. If any discrepancy between the electronic database and admission books for HCU and ICU was found, either in urgency or type of surgery, the relevant chart in question was also collected from medical records and reviewed for clarification. Data in the medical folders were collected from the anaesthesia chart, neurosurgical pre- and postoperative notes, HCU and ICU nursing notes and observation charts, as well as radiological reports where applicable. The data was captured on an electronic case report form (CRF) in Excel format.

Statistics

Descriptive statistics (numbers and percentages) with 95% confidence intervals (CI) where applicable were used to analyse the primary objective outcomes (major complication incidence).The secondary objective explored the association between possible risk factors and postoperative complications were analysed using descriptive statistics (numbers, percentages and interquartile ranges), Chi square test, Fisher's exact test, the Mann-Whitney U test and ROC analysis. A P-value of less than 0.05 was considered significant.

Results

A total of 202 consecutive patients were identified who had an elective craniotomy during the period beginning March 2016 to end February 2018. Data analysis eventually included 189 patients. The reason for the 13 patients' exclusion were due to prolonged postoperative intubation or ventilation, inadequate medical notes or missing medical folders. (Figure 1).

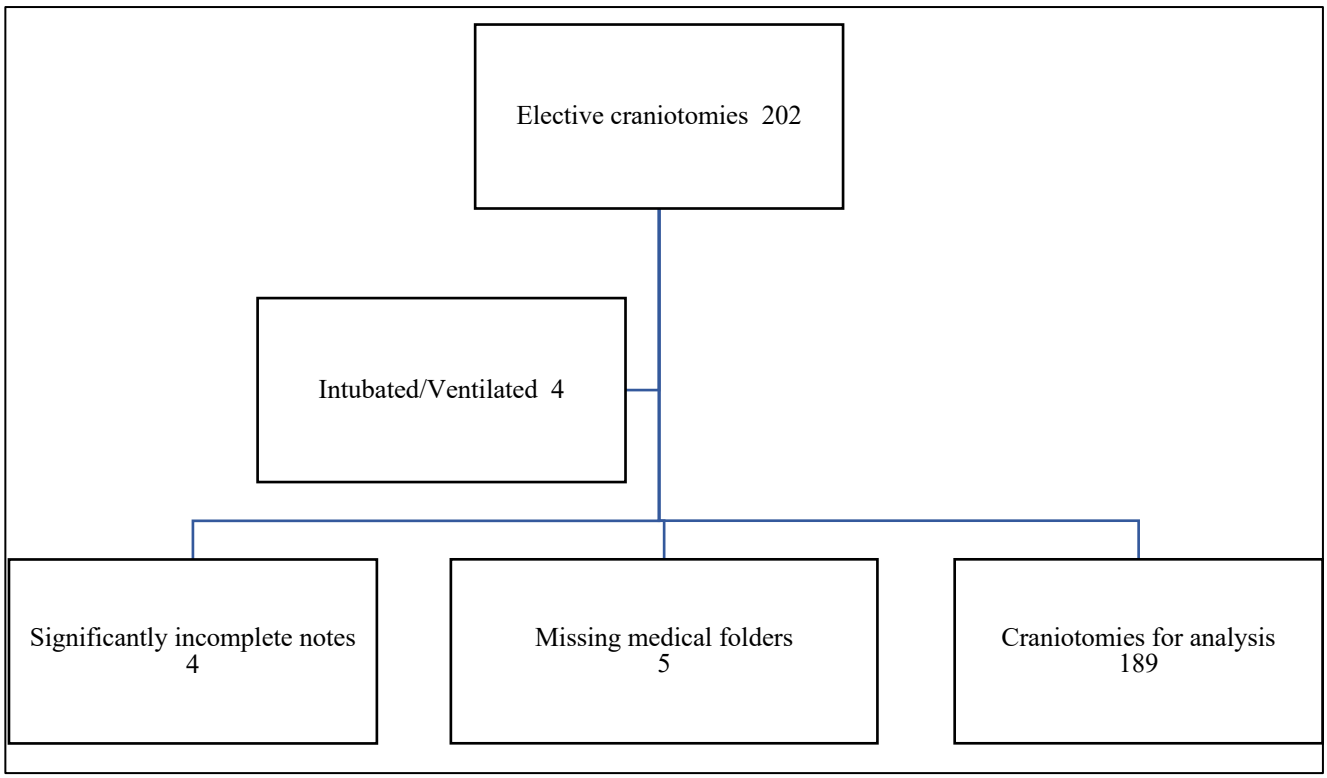

Figure 1: Study diagram of craniotomies performed

The indications for elective craniotomies performed during this audit period consisted of 164/189 (87.3%) tumour related, 12/189 (6.3%) aneurysm clipping procedures and 13/189 (6.9%) other-non-tumour* related surgery.

Tumour surgery included meningiomas (76/189 ; 40.2%), glial tumours (30/189; 15.9%), schwannomas (13/189 ; 6.9%), vascular tumours (9/189 ; 4.8%), craniopharyngiomas (7/189; 3.7%), pituitary adenomas (7/189 ;3.7%), other-tumour* related (7/189: 3.7%) and metastatic tumours (15/189 ; 7.9%).

**Please see addendum A for further information.*

Table 1.
Comparison of the incidence of specific complications within the first 6 postoperative hours of observation and the subsequent 18hrs (6-24hrs)

	Whole cohort n(%)	6hrs postoperative n (%)	6-24hrs postoperative n (%)
GCS > 2 points below baseline	9/189 (4.8%)	8/9 (88.9%)	1/9 (11.1%)
New onset motor deficit	28/189 (14.8%)	25/28 (89,3%)	3/28 (10.7%)
Seizures	4/189 (2.1%)	2/4 (50%)	2/4 (50%)
Diabetes Insipidus	1/189 (0.5%)	0/1 (0%)	1/1 (100%)
Intubation/Ventilation	4/189 (2.1%)	3/4 (75%)	1/4 (25%)
Haemodynamic instability (requiring IV drug administration)	1/189 (0.5%)	1/1 (100%)	0/1 (0%)
Acute hypertension (requiring IV drug administration)	0	0	0
Number of complications	47	39	8
Number of patients with onset of first complication	37	31	6
Death	0	0	0

Note: Incidence of complications in this table, not incidence of patients with complications. Some patients had more than one complication.

In this study 37/189 (19.6%) patients developed one or more major complications during the initial 24 hour postoperative period. Of these 37 patients, 31 (83.8%; 95% CI 71.9-95.7) patients developed their first onset complication within six hours of admission to the HCU or ICU, and the remaining 6 (16.2%; 95% CI 4.3-28.1) in the subsequent 18 hours.
(Table 1 shows incidence of specific complications within specific time frame).
Therefore, the incidence of an initial presentation of complications after six hours was 6/158 (3.9%; 95% CI 1.6-8.5). Patients who presented with their first complication after six hours postoperatively included: one patient with diabetes insipidus, one patient with seizures, one patient with a fall in GCS of more than two baseline points and three patients with a new focal neurological deficit. A further two patients who experienced a new complication after six hours, had already presented with another complication in the first six hours.

Four patients required ventilatory support within the 24-hour postoperative period. One patient was transferred intubated from theatre to the ICU, but was extubated within one hour of admission. This specific patient also represented the 1/189 (0.5%) who required inotropic support for haemodynamic instability. No patients in this audit received non-invasive ventilatory support. No deaths occurred during the initial 24 hr observation period.

Table 2.
Associations between patient characteristics and perioperative data, and postoperative complications

	No complications	Complications	p-value	Test
Age in years :mean (SD)	46,4 (14.3)	47,8 (11.8)	0.586	T-Test
n/total female (%)	93/115 (80.9%)	22/115 (19.1%)	0.853	Fisher's Exact Test
n/total male (%)	59/74 (79.7%)	15/74 (20.3%)		
Comorbidities: n (%)				
Hypertension	56/152 (36.8%)	16/37 (43.2%)	0.572	Fisher's Exact Test
Cardiovascular disease	9/152 (5.9%)	2/37 (5,4%)	0.904	Pearson Chi-Square
Pulmonary disease	11/152 (7.2%)	4/37 (10,8%)	0.471	Pearson Chi-Square
Diabetes Mellitus	15/152 (9.9%)	1/37 (2.7%)	0.160	Pearson Chi-Square
Other*	49/152 (32.2%)	10/37 (27%)	0.693	Fisher's Exact Test
Smoker[#] (n=61)	48/152 (32.6%)	13/37 (39,3%)	0.698	Fisher's Exact Test
GCS <15/15 pre-op	19/152 (12.5%)	6/37(16,2%)	0.746	Pearson Chi-Square
Speech disorder	10/152 (6.6%)	5/37 (13,5%)	0.162	Pearson Chi-Square
Motor deficit	63/152 (41.4%)	22/37 (59.5%)	0.065	Fisher Exact Test
Seizure disorder	48/152 (31.6%)	11/37 (29.7%)	1.000	Fisher Exact Test
Preoperative steroids	62/152 (40.8%)	11/37 (29.7%)	0.260	Fisher Exact Test
Anaesthesia type				Pearson Chi-Square
Inhalational agents	145/152 (95.4%)	33/37 (89.2%)	0.075	
TIVA/Awake	7 (4.6%)	4 (10.8%)		
Intraoperative vasopressor	53 (34.9%)	13/37 (35.1%)	1.000	Fisher Exact Test
Blood transfusion	11/152 (7.2%)	5/37 (13.5%)	0.219	Pearson Chi-Square
Position [@] n=188				
Lateral	5 (3.3%)	1(2.7%)	0.414	Pearson Chi-Square
Prone	12 (7.9%)	1(2.7%)		
Supine	134 (88.7%)	35 (94.6%)		
Duration[$] of anaesthesia, minutes (median, IQR), (n=188)	270 (210-330)	335 (275-420)	<0.001	Mann-Whitney U-Test

**Please see addendum A for "other" complications, #Smoker status unknown for nine patients, $Duration data inadequate for one patient, @Position data not clear for one patient*

The average patient age was 46.7 years and the interquartile range (IQR) was 35-56 years. Females represented 60.8% (115/189) of all craniotomies performed. Duration of anaesthesia was the only risk factor to have a statistically significant (P<0.05) association with overall post-operative complication incidence. The median anaesthetic time for craniotomy procedures was 285 minutes (25%-75%; 220-345 min) in this audit. Patients who developed complications in the 24 hours post-operatively had a median anaesthesia time of 342 minutes (25%-75%; 275-420 minutes) vs a median anaesthesia time of 270 min (25%-75%; 210-330 minutes) for those without complications. An anaesthetic duration of 308 minutes according to ROC curve analysis was the optimal cut point in association with post-operative complications. (Fig 2)

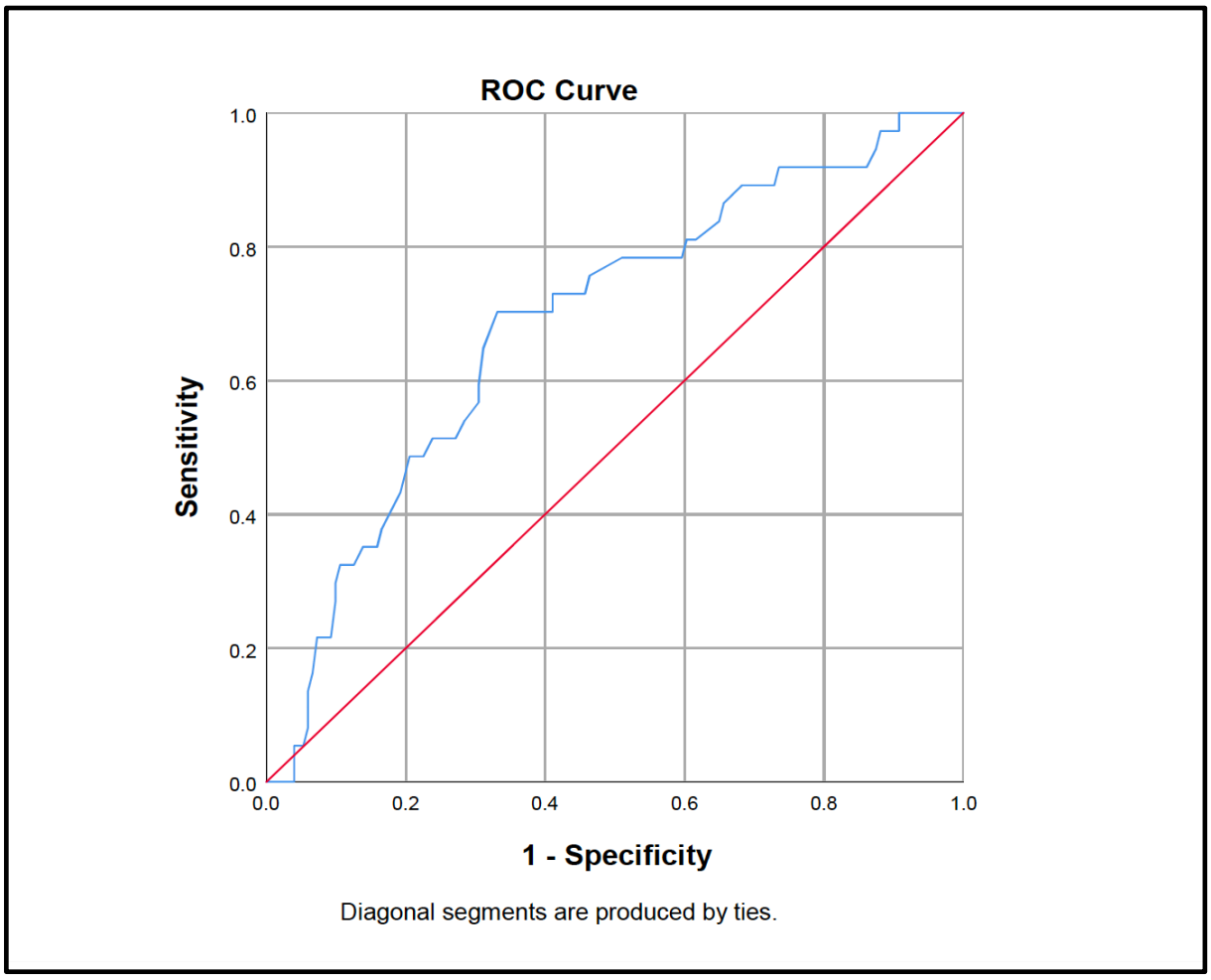

Figure 2: ROC curve for anaesthesia duration associated with post-operative complications
(area under curve 0.687; CI 0.593-0.782, p<0.001)

Discussion

Our audit highlighted that there are a significant number of patients that will suffer a major postoperative complication following elective craniotomy. Thirty-seven (19.5%) patients suffered a major complication within the first 24 hours. This percentage is slightly higher than that quoted in settings with less resource constraints (16%). This suggests that at our institution, a post-operative ICU or high care stay should be mandatory. However, of the 37 patients that developed a complication within the first 24 hours, we showed that the vast majority (31 (83.8%; 95% CI 71.9-95.7)) of these complications occurred within the first 6 hours postoperatively. This is in keeping with timing of complications in a developed country setting, where almost 90% of complications occur within this time frame. Our findings reflect that of international studies in that the majority of complications present within 6hrs.[8, 14, 15] In comparison to studies in higher income countries our audit had a greater overall neurological complication rate, specifically almost double the amount of new onset motor deficit, seizures and drop in GCS after elective craniotomies compared to de Almeida et al and Lonjaret et al.[14, 16] In a resource constrained setting such as ours, we postulate that there are a few reasons for this. One may be due to delayed presentation or diagnosis and thus more advanced pathology than that seen in resource rich countries. Another is that GSH is not a dedicated centre that deals solely with neurosurgical cases and thus we are not exposed to the pathologies as regularly as a dedicated centre would be. As pointed out in our review of the literature, the advancement of neurosurgical techniques and intra-operative anaesthetic management has improved outcomes significantly in the neurosurgical population. Therefore, in order to ensure we minimise risk of postoperative complications, we need to first ensure that we are meeting the worldwide standards of intra-operative neurosurgical care. The fact that our audit shows that we had a greater neurological complication rate warrants further investigation which is out of the scope of this audit. While the percentage of serious complications that occurred in the subsequent 18 hours is small, it is not insignificant (6/158 (3.9%; 95% CI 1.6-8.5)). The reflex would therefore be to continue current practice in order to act upon these potential complications.

However, when we delve into the type of complications that occurred in the postoperative period, it is also clear that in the majority of cases, the complications that were immediately life threatening (defined as requiring ventilatory and/or haemodynamic support) occurred within the first 6 postoperative hours. Moreover, these life threatening complications were all preceded by another complication or “red flag”, namely a drop in baseline GCS by more than 2 points or a new focal neurological deficit.

Should all non-complicated patients be discharged after the initial 6hr post-operative observation period to a neurosurgical ward, there would be a "miss" of one complication for every 26 patients discharged in the subsequent 18 hours.
In our audit, these complications included a drop in GCS, new neurological deficit, seizures and one patient with diabetes insipidus. It is the authors' opinion that these complications would be picked up timeously in a general neurosurgical ward (assuming that standard neurological observations are adhered to). Even in the case of diabetes insipidus, if routine input and output monitoring protocols are followed, this complication should be picked up. While it is a serious complication, it is also not immediately life threatening and is commonly encountered in general wards in our institution.
In an ideal world, every patient would receive postoperative care in a high care unit for as much time as it takes until the treating team feels comfortable to step down the level of care. However, when we take our context into account, this is clearly not feasible and not in the best interests of our patient population as a whole. While we are not dismissing the risk of a postoperative complication occurring after the initial 6 hour postoperative period, we believe that it is still safe to discharge patients after this time period, should all neurological and other physiological parameters be within the pre-operative baseline. This will allow for better patient turnover, higher availability of high care beds for those that need organ support and importantly will result in cost efficiency and hopefully a return to a better quality of life for patients requiring elective craniotomies but are delayed due to lack of high care bed availability.

The secondary outcome of this study showed that complications after elective craniotomies are difficult to predict from patient pre- or intra-operative characteristics, but that duration of anaesthesia might be a contributing factor. In our audit, an anaesthestic time of more than 308 min was associated with increased postoperative complications. Previous work in patients having elective craniotomies, found that surgical procedure duration has been significantly associated with complications. Anthofer et al demonstrated duration of surgery (>210 min) being significantly correlated with medical VTE, severe infection and duration of ICU stay[17]; and Rhondali et al found that a surgery time of more than 240 min to be statistically associated with mainly neurological complications postoperatively.[8] The systematic review by de Almeida et al found that along with blood loss and lateral position, duration of surgery was an independent risk factor for a postoperative complication. Duration of procedure as an independent predictor of postoperative complications should not come as a surprise as longer duration likely reflects higher complexity of the case due to unanticipated difficult access to the tumour due to its location, morphology and size, significant bleeding resulting in changes in fluid status and the need for blood products.

The same systematic review also suggested that patient positioning (especially the lateral position) was a predictor for postoperative complications. In our audit, the vast majority (more than 90%) of the patients were operated on in the supine position. We found no correlation between patient positioning and risk of postoperative complications. However, other larger studies and a systematic review, did show a correlation and thus we recommend to consider these patients at higher risk than those operated on in the supine position.

Based on our findings above, we feel that it is reasonable that carefully selected patients that arrive in a stable condition in the high care unit, following an uncomplicated procedure of duration less than 4 hours, should be considered for discharge after an uncomplicated 6 hour observation period.

If our institution were to decide to implement a non-mandatory 24 hour high care stay, consideration should be given to instituting a SOP such as that described by ter Laan et al whereby neurosurgeon, anaesthetist and nursing staff are aligned with regard to perioperative risk stratification of elective neurosurgical cases. [18] In their study, the attending neurosurgeon or anaesthetist could decide whether a patient warranted high care admission based upon high risk patient, anaesthetic or surgical factors as well as a mandatory 1 hour postoperative monitored stay in a recovery room with trained staff. This was obviously undertaken in a well-resourced environment at a dedicated centre with appropriately trained staff that are accustomed to a high turnover of elective cases. We do not enjoy the same luxuries which will make the logistics of implementation potentially onerous. One solution could be to mandate a 6 hour postoperative high care stay, at which time the patient is reviewed by a neurosurgical registrar who would then discuss with their consultant for de-escalation to a neurosurgical ward. This will allow for less unwarranted occupation of high care beds and less strain on high care staff. Moreover, it has the potential of being a significant cost containing measure which is an important factor in our resource-constrained environment.

The retrospective nature of this audit was an important limitation, especially relating to the reviewing of charts. In this audit, three patients who had new onset neurological deficit documented after six hours of admission in the nursing notes, had no doctor's notes for the initial six hours of admission with which to compare. Nursing notes were used to screen for complications when doctor's notes were not available for the first six hours of admission. GCS estimation in general was unfortunately lower in nursing notes compared to doctor's notes and motor deficits were often not documented in the nursing notes when it was documented in doctor's during the same time frame.

The chart review limitation also had an impact on the analysis of the secondary outcome of our study. Due to documentation clarity, anaesthesia time, instead of surgical time was recorded and analysed in our study.

Future prospective studies of this nature in low- and middle-income countries are needed. The tendency for higher neurological complications postoperatively needs to be further investigated, and hopefully pre-operative risk stratification can be better adapted for earlier discharge observation periods, in this uniquely resource-constrained health system.

Conclusion

Initial complications presenting six hours after admission following elective craniotomies in our audit were neither life threatening, nor should require more than standard neurosurgical ward observations to direct further management.

Consideration should be given, in a resource constrained environment, to discharge elective craniotomy patients from a HCU or ICU to a neurosurgical ward after an initial uncomplicated six hours. A high probability to develop diabetes insipidus might be a special consideration for longer observation times.

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Appendixes

A. Addendum A : Craniotomy surgery indications and "other" comorbidities

Craniotomy indications

Aneurysms	Craniopharyngioma	Glial Tumours	Vascular Tumours		Meningion	Metastatic	Pituitary Adenor	Schwannoma	Other		Total
12	7	30	9		76	15	7	13	20		189
			Haemangioma	*2*					*Arachnoid Cyst*	*1*	
			Haemangioblastoma	*3*					*Dysplasia (cortical dysplasia in seizures)*	*1*	
			Haemangiopericytoma	*4*							
									Epidermoid cyst	*4*	
									Inflammatory lesion (other)	*4*	
									Other (not specified)	*2*	
									Syringomyelia	*1*	
									Total	*13*	
									"Other-tumour"		
									Ependyoma	*1*	
									Epstein-Barr-V smooth muscle tumour (other)	*1*	
									Giant cell tumour	*1*	
									Low grade neoplasm (other)inconclusive path dx	*1*	
									Lymphoma	*2*	
									Paraganglioma	*1*	
									Total	*7*	

"Other" comorbidities

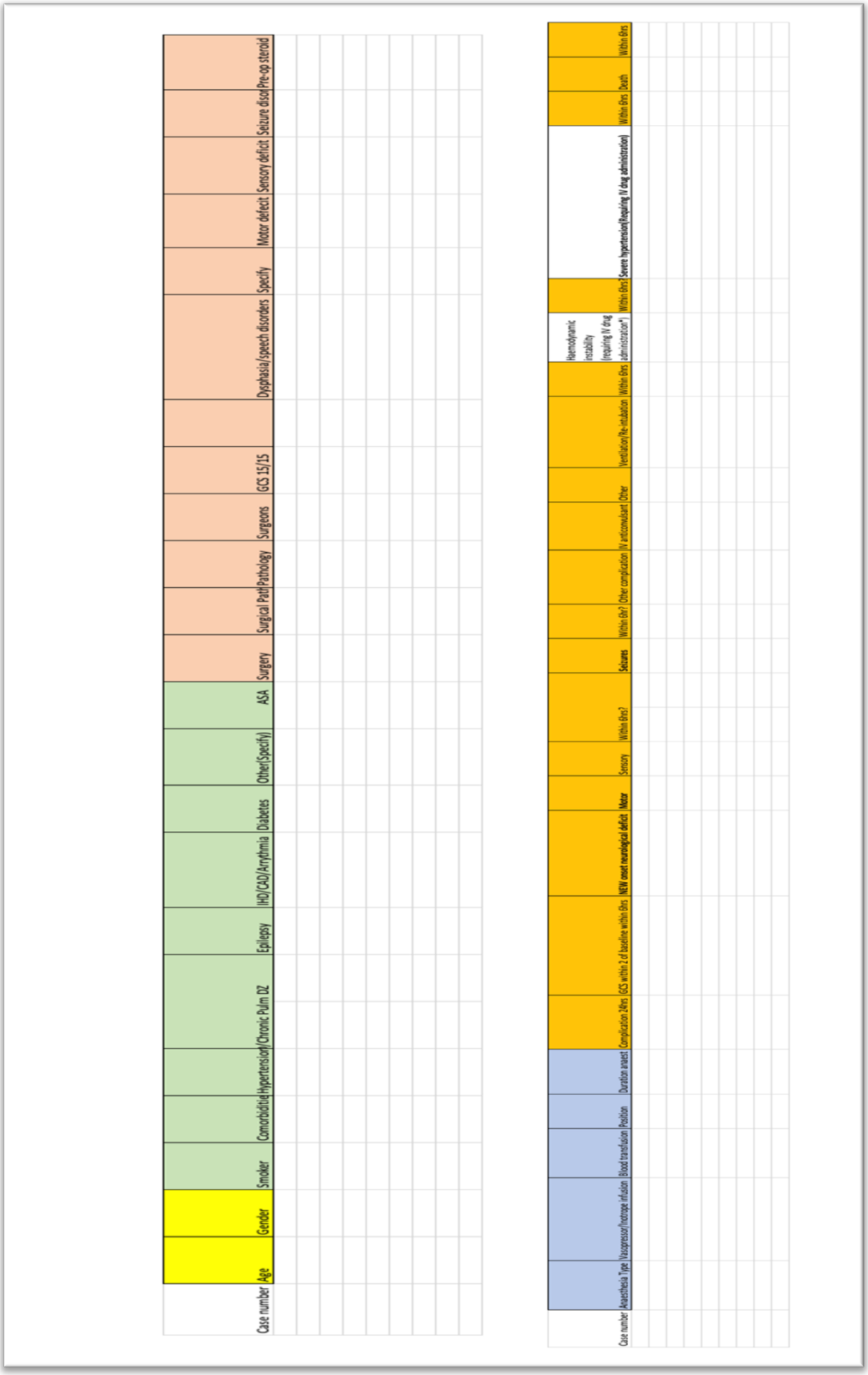
Other comorbidities
Hypercholesterolaemia
Sarcoidosis
Hemophilia A
Neurofibromatosis
Morbid obesity
Human Immunodeficiency Virus
Hypothyroidism
Hyperthyroidism
Pulmonary hypertension

B. Glasgow Coma Scale

Glasgow Coma Scale

Best eye response (E)	Spontaneous – open with blinking at baseline	4
	Opens to verbal command, speech, or shout	3
	Opens to pain, not applied to face	2
	None	1
Best verbal response (V)	Oriented	5
	Confused conversation, but able to answer questions	4
	Inappropriate responses, words discernible	3
	Incomprehensible speech	2
	None	1
Best motor response (M)	Obeys commands for movement	6
	Purposeful movement to painful stimulus	5
	Withdraws from pain	4
	Abnormal (spastic) flexion, decorticate posture	3
	Extensor (rigid) response, decerebrate posture	2
	None	1

C. Case report form (Excel format)



IHD: Ischaemic Heart Disease
CAD:Coronary artery disease
IV: Intravenous

D. Ethics approval letter

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: sumayah.ariefdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

06 March 2018

HREC REF: 857/2017

Dr A Reed
Division of Anaesthesia
D-23
NGSH

Dear Dr Reed

PROJECT TITLE: ELECTIVE CRANIOTOMY OBSERVATIONAL STUDY: (ECO STUDY) (MMeD-candidate-Dr C Claassens)

Thank you for your response letter dated 01 March 2018, addressing the issues raised by the Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 March 2019.

The HREC note that this is a new retrospective audit for 2 years going backwards from 05/03/2018.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the student: Dr C Claassens will also be involved in this study.

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

Signature Removed

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.

HREC:857/2017

Institutional Review Board (IRB) number: IRB00001938
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI),and Declaration of Helsinki (2013) guidelines.
The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

HREC:857/2017

E. Author's guidelines for manuscript submission

(African Journal Of Thoracic and Critical Care Medicine)

Author Guidelines

Author Guidelines

Please view the Author Tutorial for guidance on how to submit on Editorial Manager.

To submit a manuscript, please proceed to the *AJTCCM* Editorial Manager website:
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To access and submit an article already in production, please see the guidelines here.

Author Guidelines

Please take the time to familiarise yourself with the policies and processes below. If you still have any questions, please do not hesitate to ask our editorial staff (tel.: +27 (0)21 532 1281, email: submissions@hmpg.co.za).

General article format/layout

Submitted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction prior to being sent for review, which will delay publication.

General:

- Manuscripts must be written in UK English (this includes spelling).
- The manuscript must be in Microsoft Word document format. Text must be 1.5 line spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes). Pages and lines should be numbered consecutively.
- Please make your article concise, even if it is below the word limit.
- Qualifications, ***full*** affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.
- Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.
- Scientific measurements must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dL).
- Litres is denoted with an uppercase L e.g. 'mL' for millilitres).
- Units should be preceded by a space (except for % and ºC), e.g. '40 kg' and '20 cm' but '50%' and '19ºC'.
- Please be sure to insert proper symbols e.g. µ not u for micro, a not a for alpha, b not B for beta, etc.
- Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160.
- Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.

If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the *only* exception. Please DO NOT use fill, format lines and so on.

IMAGES/PHOTOGRAPHS

Acceptable file types

The image file should be submitted as a high resolution jpeg or tiff Important: Images embedded in a Word document are not acceptable.

Resolution

Images must have a minimum resolution of 300 dpi (dots per inch).

Screenshots and images from the internet

Screenshots and images from the internet are usually only 72 dpi – this is the average resolution that computer screens use – therefore images downloaded from the internet are almost always too small to use for print even though they might look fine on screen.

Author Quick check

If the actual size of the file is:

• less than 500 kb - not great for print

• 500kb - 1000 kb (1 mb) - better

• greater than 1000 kb (i mb) - ideal

The image sent has to be the original i.e. the very first image created.

If it was taken on a camera/cell phone, then that image has to be sent directly from the device's image gallery.

Not a screenshot of the image or via a secondary app (Word, Whatsapp) or uploaded to a website.

Cameras (cell phones) should be set to the highest possible image size

GRAPHS/FIGURES

Acceptable file types

All graphs and figures should be submitted as PDF files

Preparation notes by article type

Research

Guideline word limit: 3 000 words (excluding abstract and bibliography)

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Where appropriate, sample size calculations should be included to demonstrate that the study is not underpowered. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

- May include up to 6 illustrations or tables.
- A max of 20 – 25 references

Structured abstract

- This should be no more than 250words, with the following recommended headings:
  - **Background:** why the study is being done and how it relates to other published work.
  - **Objectives:** what the study intends to find out
  - **Methods:** must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.
  - **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
  - **Conclusion:** must be supported by the data, include recommendations for further study/actions.
  - Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors. It should be able to be intelligible to the reader without referral to the main body of the article.
  - Do not include any references in the abstracts.

Illustrations/photos/scans

- If illustrations submitted have been published elsewhere, the author(s) should provide evidence of consent to republication obtained from the copyright holder.
- Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'.
- Each figure must have a caption/legend: Fig. 1. Description (any abbreviations in full).
- All images must be of high enough resolution/quality for print.
- All illustrations (graphs, diagrams, charts, etc.) must be in PDF form.
- Ensure all graph axes are labelled appropriately, with a heading/description and units (as necessary) indicated. Do not include decimal places if not necessary e.g. 0; 1.0; 2.0; 3.0; 4.0 etc.
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- Each image must be attached individually as a 'supplementary file' upon submission (not solely embedded in the accompanying manuscript) and named Fig. 1, Fig. 2, etc.

Tables

- Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged.
- Large tables will generally not be accepted for publication in their entirety. Please consider shortening and using the text to highlight specific important sections, or offer a large table as an addendum to the publication, but available in full on request from the author.
- Embed/include each table in the manuscript Word file - do not provide separately as supplementary files.
- Number each table in Arabic numerals (Table 1, Table 2, etc.) consecutively as they are referred to in the text.
- Tables must be cell-based (i.e. not constructed with text boxes or tabs) and editable.
- Ensure each table has a concise title and column headings, and include units where necessary.
- Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

Do not: Use [Enter] within a row to make ‘new rows’:

Rather:
Each row of data must have its own proper row:

Do not: use separate columns for *n* and %:

Rather:
Combine into one column, *n* (%):

Do not: have overlapping categories, e.g.:

Rather:
Use <> symbols or numbers that don’t overlap:

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NB: *Only complete, correctly formatted reference lists in Vancouver style will be accepted. If reference manager software is used, the reference list and citations in text are to be unformatted to plain text before submitting..*

- Authors must verify references from original sources.

- Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others.[3,4-6]
- All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order).
- Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus.
- Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al.
- Volume and issue numbers should be given.
- First and last page, in full, should be given e.g.: 1215-1217 **not** 1215-17.
- Wherever possible, references must be accompanied by a digital object identifier (DOI) link). Authors are encouraged to use the DOI lookup service offered by CrossRef:
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As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

1. Named authors consent to publication and meet the requirements of authorship as set out by the journal.
2. The submission has not been previously published, nor is it before another journal for consideration.
3. The text complies with the stylistic and bibliographic requirements in **Author Guidelines**.
4. The manuscript is in Microsoft Word or RTF document format. The text is single-spaced, in 12-point Times New Roman font, and contains no unnecessary formatting.
5. Illustrations/figures are high resolution/quality (not compressed) and in an acceptable format (jpeg or pdf). These must be submitted individually as 'supplementary files' (not solely embedded in the manuscript).
6. For illustrations/figures or tables that have been published elsewhere, the author has obtained written consent to republication from the copyright holder.
7. Where possible, references are accompanied by a digital object identifier (DOI).
8. An abstract has been included where applicable.
9. The research was approved by a Research Ethics Committee (if applicable)
10. Any conflict of interest (or competing interests) is indicated by the author(s).