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Type A acute aortic dissection repair during night time: should we delay surgery to the following morning?

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Abstract

Background: Out-of-hours work is believed to lead to a higher complication rate and mortality after surgery. However, there is no data supporting this perception in type A acute aortic dissections (TAAD) repair. We present an observational study of prospectively collected data comparing operative outcomes and late survival of TAAD repair performed after hours versus regular daytime working hours.

Methods: A total of 196 patients undergoing emergency TAAD repair (mean age 59 ± 13 years, range 18-81, F/M 57/139,) were included in the final analysis. Patients were stratified **a**s **D**ay-time between 7 AM and 7 PM (n=124), and **N**ight-time between 7 PM and 7 AM (n=72). Inverse Propensity Score (PS) weighting for modelling causal effects was used to assess the effect of time procedure on outcomes of interest.

Results: Overall 30 day mortality was 14.3% (28 patients). No significant differences were found between the night-time and day-time groups with regards to operative mortality (8.3% versus 17.3%; adjusted OR 0.35; 95%CI 0.12-1.04; P=0.06), re-exploration (12.5% versus 9.7%; adjusted OR 2.09; 95%CI 0.72-6.07; P=0.18) and neurological deficit (18.1% versus 16.9%; adjusted OR 0.91; 95%CI 0.33-2.54; P=0.87). Long term survival at mean 9 years follow-up was comparable between the two groups (adjusted long-rank P=0.28).

Conclusions: Night-time surgical repair of TAAD when compared with Day-time repair does not seem to be associated with a greater risk of surgical complications, operative mortality and long term mortality.

Introduction

The causes of medical errors are often multifactorial, however, medical staff fatigue associated with delivering ~~medical~~ care outside daytime working hours is an important recognised driving factor [1-4].

It has been previously suggested that out-of-hours work leads to higher complication rate and mortality after surgery; surgeon fatigue, decreased availability of support staff, and other logistical factors are believed to play an adverse role [3,4]. However, recent large observational studies on non-cardiac ~~operations~~ ~~procedures~~ failed to demonstrate an adverse effect of night time operations [5-7]. Moreover very limited data are available regarding night time work and adverse outcomes in cardiac surgery [8-10].

It is common practise in type A acute aortic dissections (TAAD) to proceed to surgery without delay even in the presence of clinical stability given the potential for catastrophic rupture [11]. This results in a large number of cases performed during night time. However, the perception that after-hours surgery may be associated with poorer outcomes remains, and surgery is occasionally postponed to the following morning. To date no previous study has investigated the impact of night time operation in TADD repair ~~with relative lack of definitive consensus~~.

Here, we present the results of an observational study comparing operative outcomes and late survival of TAAD repair performed during Day-time and Night-time working hours.

METHODS

Data Sources and Study Population

The study was conducted according to the principles of the Declaration of Helsinki. The local audit committee approved the study and the requirement for individual

patient consent was waived. Data prospectively collected were extracted from the Bristol Heart Institute (BHI) PATS system for all patients who required urgent/emergent repair of TAAO from 1992 to 2014 ~~with information regarding operative time available~~ (n=209).

Patients presenting with cardiogenic shock for any cause were excluded (n=13) leaving a total of 196 patients (mean age 59±13 years, range 18-81, F/M 57/139) included in the final analysis. Patients were stratified by operative time: Day-time was defined between 7 AM and 7 PM (n=124) and Night-time between 7 PM and 7 AM (n=72).

Definitions

Type A Aortic dissection was classified according to the Stanford system where type A dissection involves the ascending aorta. Acute dissection was defined by onset of symptoms within 14 days of operative treatment. Malperfusion syndromes were defined according to symptoms from each arterial system and required clinical evidence of lack of blood flow to defined organ system. That included: cerebral/spinal malperfusion — stroke, paraplegia; cardiac malperfusion — EKG changes, CK or troponin elevation — myocardial dysfunction; iliofemoral malperfusion — loss of pulses, sensory, or motor function; renal malperfusion — creatinine elevation, lack of urine output; mesenteric malperfusion — abdominal tenderness, bowel ischemia, elevation of liver function tests. Evidence of dissection flap in branch vessels, either surgically or radiographically without symptoms of malperfusion, was not considered as malperfusion syndrome.

Surgical procedure

Femoral arterial cannulation was the preferred choice for establishment of cardiopulmonary bypass (90%) with axillary cannulation and direct aortic used in the

remaining 10% of cases. Deep hypothermic circulatory arrest was used in all cases and selective antegrade cerebral perfusion in 22(11.2%) patients.

Outcomes of interest

Short term outcomes investigated were 30 ~~day mortality~~day mortality, postoperative neurological deficit, low output syndrome and re-exploration for bleeding. All-cause mortality was used as long-term outcome which represents the most robust and unbiased index in retrospective analysis ands it avoids inaccurate and biased documentation and clinical judgment. Information about death is obtained from the National General Register Office approximately 1 week after the event.

Statistical analysis

For baseline characteristics, variables are summarised as mean \pm standard deviation for continuous variables and percentage for categorical variables. The chi squared test was used to test unadjusted association between treatment variable and outcomes. Multiple imputation ($m=3$) was used to address missing data. Rubin's method [12] was used to combine results from each of m imputed data sets.

Inverse Propensity Score weighting (IPSW) for modelling causal effects was used to assess the effect of Night-time versus Day-time procedure on outcomes of interest [13]. For this purpose, a generalised boosted model (GBM) was implemented to estimate individual propensity scores (PS) adjusting for 12 pre-treatment covariates including age, female gender, left ventricular ejection fraction ~~less than~~ $\leq 50\%$, hypertension, peripheral vascular disease, previous cardiac surgery, malperfusion syndromes, aortic arch involvement, time from symptoms onset to surgery and time from diagnosis to surgery.

To estimate the average treatment effect on the treated (ATT) For ATT, we give each Night-time case a weight of 1 and each Day-time case a weight $w_i = p(x_i)/(1-p(x_i))$. The absolute standardised mean difference (ASMD) was used as a balance metric to summarize the difference between two univariate distributions of a single pre-treatment variable. A value ≥ 0.20 was considered as an indicator of imbalance [14]. Effective sample size (ESS) in the weighted samples was calculated to account for the potential loss in precision from weighting. We then estimated the treatment effect with a weighted logistic regression model for operative outcomes and logrank test for late mortality that contained only the treatment indicator (night time versus day time). As sensitivity analysis, the effect of operative time on operative mortality was tested as continuous variable in a PS weighted adjusted spline analysis. R version 3.1.2 (2014-10-31) was used for all statistical analysis.

Results

Pre-treatment variables distribution and operative data

Table 1 summarises pre-treatment variable distribution between Night-time versus Day-time group. Overall, patients who underwent surgery during the Day-time presented a higher risk profile including female gender, previous cardiac surgery procedure and hypertension. The incidence of malperfusion syndromes were not significantly different between the two groups. A trend towards a longer time from onset of symptoms to surgery and time from diagnosis to surgery was present in the Day-time group. After inverse PS-weighting the two groups were comparable for all pre-treatment variables. Operative data are summarized in Table 2. The two groups did not differ for all intraoperative variables analysed.

Effect of night time on outcomes

Crude operative outcomes and unadjusted PS-adjusted Night-time effects are summarised in Table 3. Overall 30 days mortality was 14.3%, (28 patients). No significant differences were found between the Night-time and Day- time groups with regards to operative outcomes investigated.

After a mean follow-up time of 7.9±6.5 years [max 0-23] crude survival probability at 1, 5, and 15 was 89±4% versus 81±4%, 84±4% versus 77±4%, 70±6% versus 57±5% and 58±7% versus 46±6% in the Night-time and Day-time groups respectively (long-rank P=0.12, Figure 1, right). In the propensity score weighted sample mean follow-up time was 9 years. PS weighted survival probability at 1, 5, and 15 was 89±4% versus 78±17%, 84±4% versus 75±18%, 70±6% versus 58±23% and 58±7% versus 51±26% in the Night-time and Day-time groups respectively (long-rank P=0.28, Figure 1, left).

Effect of Operative time as continuous variable on mortality

In a PS weighted spline analysis, operative time considered as continuous variable was not significantly associated with operative mortality (P=0.28) but hourly variations in mortality during the 24-hour period were noted (Figure 2).

Discussion

To our knowledge, this analysis represents the only study to date investigating the association of operative time of day with outcomes in type A acute aortic dissection repair. Night-time repair did not increase operative mortality or postoperative complications including re-exploration, incidence of postoperative neurologic deficit or low output syndrome. Furthermore, Night-time operations did not affect late survival. Surprisingly, hourly variations in mortality during the 24-hour period were noted with a trend toward a lower mortality rate during the night hours. This trend might be partially related to the residual imbalance regarding the prolonged time from symptom onset to surgery in the Day-time group. Such a delay might be responsible for prolonged organs malperfusion thus leading to poorer operative outcomes.

Although specific information regarding the reasons for prolonged time from symptoms onset to surgery in the Day-time group were not available, we can speculate that this might be partially explained by delayed operations for night-time admissions. In addition, during Day-time operative rooms are usually occupied with elective surgeries which may further delay the emergency case. Finally, we found a higher prevalence of previous cardiac operation in the Day-time group. Previous sternotomy is commonly believed to be a protective factor for imminent rupture and these cases are more likely to be postponed to the following morning. On the other hand, previous sternotomy can affect operative outcomes with its relative technical complexity.

Although operative mortality is ultimately the most important outcome measure, a detailed examination of secondary outcomes is crucial to understanding the potential adverse effects if any, associated with Night-time surgery repair. We also found that

the incidence of postoperative complications was comparable between the two groups with only a mild increase in re-exploration for bleeding in patients undergoing repair at night. Postoperative bleeding requiring reoperation is not an uncommon complication after surgery for aortic dissection. Theoretically, surgical fatigue could lead to careless technique, resulting in additional bleeding requiring reoperation. However, the absolute difference we observed was small and unlikely not to be of clinically significant.

Acute aortic dissection repair is associated with increased technical complexity and mortality rate. In this context, the potential reduction in performance during night time secondary to fatigue, intraoperative shift changes, technical lapses and decreased situational awareness is anticipated to have an impact on operative outcomes [1-4]. This perception occasionally leads surgeons to delay surgery to the following morning in particular in cases of clinical stability. Contrary to the common belief, we found operative time of day not to be associated with TAAD repair worse operative outcomes and long term survival.

Our results are supported by other recent reports on operative time and surgical outcomes. In fact, Despite extended work shifts inevitably lead to sleep deprivation and fatigue and may potentially result in reduced performance as reported for in-hospital cardiac arrest [2], the literature on the impact of night time operation on surgical outcomes and performance gives conflicting results [3,10]. A recent report from the US National Trauma Data Bank [5] (2007 to 2010) on 16,096 patients and 15,109 patients who underwent an exploratory laparotomy in the night time and day time, respectively, found no difference in the risk-adjusted mortality rate between the two groups. For thoracic organ transplantation, a large UNOS database cohort study including more than 27,000 heart and lung transplant recipients did not reveal any

significant association between night-time heart or lung transplantation and 1-year mortality [6]. An international prospective observational study on 11,290 patients from 28 European countries undergoing urgent non-cardiac surgery did not identify any relationship with the time of day at which the procedure was performed [7]. In addition, three available studies reporting on coronary artery bypass graft and valve surgery [8-10] found no significant differences in mortality or intraoperative complications in patients operated on by sleep-deprived versus non-sleep-deprived surgeons. Therefore, the common belief that surgeons perform at their best during day-time rather than in the middle of night does not seem to be consistently supported by current evidence.

As with all observational studies, a caveat of our study is the selection bias introduced by not randomizing patients to the 2 operating time groups. We have tried to minimize this bias by propensity-weighting patients using the set of patient risk factors available in our registry. Nevertheless, a remaining threat to selection bias is unmeasured factors in particular the information regarding reasons for the prolonged time from symptoms onset to surgery in the Day-time group (surgeon preference, clinical features). Furthermore, we were unable to account for surgeon-level variables such as experience, fatigue, time since last sleep, or length of shift. Finally, given the relatively small sample size, analysis on hourly variations in mortality was not conclusive; studies with larger sample sizes and longer follow-up periods are needed to confirm these findings.

In summary, contrary to the common perception, Night-time TAAD repair was not associated with a greater risk of ~~surgical complications~~, operative morbidity and long term mortality than Day-time repair. According to our results, it seems, therefore, reasonable, to suggest that TAAD repair procedures should be performed as

emergency operation regardless of the time of day. ~~This approach, is also supported in view of by~~ the reported mortality rate of 1% to 2% per hour immediately after symptom onset in historical untreated patients [11] and based on the assumption that prolonged period of organs malperfusion can affect operative outcomes. Further larger studies are required to draw definitive conclusions.

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Table 1. Pre-treatment variables distribution in the unweighted and propensity score weighted groups.

	unw	unw	unw	unw	PS-w	PS-w	PS-w	PS-w
	Night	Day	ASMD	P	Night	Day	ASMD	P
	time	time			time	time		
	N=72	N=125			N=55	N=124		
Age (yrs)	60±13	58±14	0.17	0.26	60±13	60±11	0.01	0.96
Female	24%	32%	-0.20	0.19	24%	28%	-0.10	0.58
Arch involvement	26%	23%	0.09	0.55	26%	24%	0.06	0.73
Previous cardiac surgery	4%	10%	-0.27	0.12	4%	5%	-0.03	0.87
LVEF <50%	8%	10%	-0.08	0.61	8%	8%	-0.00	0.98
Vascular disease	8%	7%	0.04	0.79	8%	6%	0.08	0.62
Hypertension	53%	64%	-0.23	0.11	53%	54%	-0.03	0.85
Marfan Diagnosis	6%	4%	0.07	0.64	6%	1%	0.18	0.16
Cerebral malperfusion	10%	10%	0.00	0.99	10%	7%	0.07	0.63
Renal malperfusion	4%	6%	-0.07	0.64	4%	4%	0.01	0.92
Mesenteric malperfusion	4%	3%	0.05	0.74	4%	2%	0.10	0.50
Iliofemoral malperfusion	10%	12%	-0.08	0.60	10%	10%	-0.02	0.90
Symptoms to surgery (h)	19±21	22±19	-0.14	0.31	19±21	18±7	0.04	0.80
Diagnosis to surgery (h)	7±6	9±9	-0.35	0.06	6±6	7±7	-0.10	0.63

unw: unweighted; PS-w: propensity score weighted; ASMD: absolute standardised mean difference; LVEF: left ventricular ejection fraction

Table 2. Operative data

	Night-time group	Day-time group	P
Aortic valve replacement %	38.9%	36.3%	0.8
Root replacement %	30.6%	21.8%	0.2
Arch replacement %	8.3%	11.3%	0.7
Cross clamp time (min)	173	174	0.9
X clamp time (min)	92	84	0.2
Selective Antegrade Cerebral Perfusion %	8.7%	11.8%	0.8

Commented [GA1]: Is this CPB time?

Table 3. Operative outcomes

	Night time	Day time	uw OR[95%CI]	uw P	PS-w OR[95%CI]	PS-w P
Mortality	8.3%	17.3%	0.40[0.15-1.04]	0.08	0.35[0.12-1.04]	0.06
Re-exploration	12.5%	9.7%	1.33[0.52-3.32]	0.54	2.09[0.72-6.07]	0.18
ND	18.1%	16.9%	1.08[0.49 2.29]	0.84	0.91[0.33-2.54]	0.87
LOS	15.3	16.9	0.88[0.38-1.93]	0.76	0.93[0.72-6.07]	0.88

unw: unweighted; PS-w: propensity score weighted; OR: odds ratio; CI: confidence interval; ND: neurological deficit; low output syndrome

Figure Legends

Figure 1. Day-time and Night-time Survival of **I**type A acute aortic dissection repair in the unweighted (right) and propensity score weighted samples.

Figure 2. Relationship between operative mortality and operative time (weighted regression)

