NICE thromboprophylaxis guidelines are not associated with increased pericardial effusion after surgery of the proximal thoracic aorta

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ABSTRACT

INTRODUCTION In 2010 the National Institute for Health and Clinical Excellence (NICE) released guidelines on venous thromboembolism. Strategy focused on risk assessment, antiembolic stockings, sequential compression devices, subcutaneous high dose enoxaparin (40mg), early mobilisation and hydration. The 40mg enoxaparin dose over the previous 20mg regimen was worrisome, and its effect on pericardial effusion rates and mortality in proximal aortic surgery was investigated.

METHODS Proximal aortic reconstructions performed between December 2008 and April 2011 were identified from prospectively collected data in a tertiary centre database. Retrospective analysis of patient notes was performed. Proximal aortic surgery patients were categorised as low dose (20mg) enoxaparin and high dose (40mg) enoxaparin, and compared for confounding variables. In-hospital, early and one-year readmission rates for pericardial effusion were ascertained from echocardiography reports. The primary outcome was total pericardial effusion rate. Secondary outcomes consisted of 30-day and 1-year mortality.

RESULTS A total of 198 patients underwent proximal thoracic aortic surgery. Nine patients were excluded due to early post-operative death ($n=5$) and missing patient records ($n=4$). This left 189 cases for analysis. There were 93 patients in the low dose group and 96 in the high dose group. Groups were comparable for age, cardiopulmonary bypass time, aortic cross-clamp time, postoperative warfarin and antiplatelet agents. Pericardial effusion rates up to one year were comparable (low dose 19% vs high dose 21%). Thirty-day mortality was lower in the low dose group (0 vs 3 deaths). There were four deaths up to one year but these were not attributable to increased enoxaparin.

CONCLUSIONS Increased perioperative thromboprophylaxis dosage does not increase pericardial effusion rates or mortality in proximal aortic surgery.

KEYWORDS

Aortic operations – Bleeding – Echocardiography – Pericardium – Surgery – Complications

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Pericardial effusion is a common complication of cardiac surgery, has been shown to compromise recovery¹ and is commonly found after proximal aortic surgery.² Cardiac tamponade may present early or late after cardiac surgery and can be difficult to diagnose due to varied clinical, haemodynamic or echocardiographic findings.

In patients undergoing coronary artery bypass grafting, valve replacement or other types of surgery, pericardial effusion has been detected in 64% of cases.³ The effusion is small in 68.4%, moderate in 29.8% and large in 1.6% of these cases. Loculated effusions have been shown to be more frequent than diffuse ones (57.8% vs 42.2%). The incidence of postoperative cardiac tamponade has been shown to be 2% following valvular, bypass and aortic surgery,⁴ and in aortic root surgery with or without aortic valve replacement, significant pericardial effusions have been shown

to develop in up to 31.6% of cases.⁵ Echocardiography has therefore been advocated routinely in the postoperative period in patients undergoing aortic root surgery to exclude significant pericardial effusion.

Percutaneous catheter drainage, blind subxiphoid pericardiotomy and open surgical drainage have all been described as effective techniques in the management of cardiac tamponade secondary to haemopericardium in patients with cardiopulmonary arrest or near cardiopulmonary arrest.^{6,7} Management techniques such as routine placement of retrocardiac closed suction drains have been shown to be effective in reducing cardiac tamponade and atrial fibrillation rates in ascending aortic surgery.⁸

The evidence with respect to the influence of antithrombotic therapy on pericardial effusion rates following cardiac surgery is scanty. In one series, echocardiography was per-

Figure 1 Flowchart for study

Table 1 Patient demographics	Enoxaparin dose		p-value
	20mg (n=93)	40mg (n=96)	
Mean age (yrs)	58 (SD: 16)	59 (SD: 16)	0.67
Mean cardiopulmonary bypass time (mins)	157 (SD: 54)	171 (SD: 70)	0.13
Mean aortic cross-clamp time (mins)	107 (SD: 37)	108 (SD: 39)	0.86
Postoperative warfarin	41 (44%)	43 (45%)	0.92
Postoperative antiplatelet therapy	64 (69%)	54 (56%)	0.08

SD = standard deviation

formed one and two weeks postoperatively after insertion of a valve prosthesis (n=50) and after coronary bypass surgery (n=100) (receiving a combination of aspirin and dipyridamole [n=50]; receiving warfarin [n=50]).⁹ The pericardial effusion rate was 77% for both procedures and pericardial effusion was marked in 29% of cases. Pericardial effusion rates were not found to be related to antithrombotic therapy type.

Venous thromboembolism (VTE) is associated with significant mortality, morbidity and healthcare implication.

Guidelines issued by the National Institute for Health and Clinical Excellence in 2010 were designed to reduce rates of VTE through mandatory VTE risk assessment, and focused on administration of antiembolic stockings, sequential compression devices, subcutaneous enoxaparin (dose 40mg), early mobilisation and hydration. However, thromboprophylaxis in the surgical setting is worrisome. In orthopaedic surgery, short duration thromboprophylaxis (1–14 days) has been shown to be associated with higher bleeding rates than

Table 2 Pericardial effusion rates

	Enoxaparin dose	
	20mg (n=93)	40mg (n=96)
In-hospital pericardial effusion	17 (18%)	16 (17%)
Early readmission for pericardial effusion	1 (1%)	2 (2%)
Management of pericardial effusion		
Conservative	13 (14%)	14 (15%)
Ultrasonography guided drainage	2 (2%)	2 (2%)
Open surgery	3 (3%)	2 (2%)
Reaccumulation after drainage	0 (0%)	0 (0%)
9-month readmission for pericardial effusion	0 (0%)	1 (1%)
Total cases of pericardial effusion	18 (19%)	20 (21%)

Table 3 Mortality

	Enoxaparin dose		p-value
	20mg (n=93)	40mg (n=96)	
30-day mortality	0 (0%)	3 (3%)	0.25
9-month mortality for pericardial effusion	0 (0%)	1 (1%)	1.00
Total mortality	0 (0%)	4 (4%)	0.12

Table 4 Type of surgery

	Enoxaparin dose		p-value
	20mg (n=93)	40mg (n=96)	
Ascending aorta replacement only	28 (30%)	35 (36%)	0.41
Ascending aorta + AVR	25 (27%)	21 (22%)	
Composite aortic root replacement (including valve sparing) ± AVR	38 (40%)	33 (34%)	
Ascending aorta ± AVR + aortic arch replacement	1 (1%)	4 (4%)	
Composite aortic root + aortic arch replacement	1 (1%)	3 (3%)	
'Redo' surgery	8 (9%)	5 (5%)	0.40
Additional procedures	13 (14%)	17 (18%)	0.55

AVR = aortic valve replacement

for those who receive thromboprophylaxis for one day following total hip replacement or total knee replacement surgery.¹⁰ The purpose of this study was to deduce whether a more aggressive thromboprophylaxis regimen exacerbated the accumulation of clinically significant pericardial effusion, increasing the potentially fatal sequelae of pericardial effusion and overall mortality.

Methods

Prospectively collected data were analysed from a tertiary referral centre cardiac surgical database to identify all proximal aortic surgical cases performed between December 2008 and April 2011. Patients who died intraoperatively were excluded. Patients were classified as having

undergone proximal aortic surgery defined as any surgery from root to arch of the aorta. Patient notes were obtained for retrospective data collection and analysis. Those with significant missing records were excluded.

Patients identified as having undergone proximal aortic surgery were categorised into two groups: low dose enoxaparin (20mg) and high dose enoxaparin (40mg). No preoperative dose of enoxaparin was given and the first postoperative dose was on the evening of the day of surgery. The groups were compared for age, cardiopulmonary bypass and aortic cross-clamp times, postoperative warfarin and antiplatelet therapy rates. In-hospital pericardial effusion rates were ascertained from postoperative echocardiography reports in those patients who underwent this investigation. Early readmission rates for pericardial effusion and

readmission rates for pericardial effusion up to one year were collated from chart review. The primary outcome was total pericardial effusion rate up to one year where the pericardial effusion was ≥ 1 cm. Secondary outcomes consisted of 30-day mortality and 1-year mortality. Individual mortality cases were reviewed by a study committee to ascertain whether death could be attributed to the enoxaparin dose.

Data were analysed with SPSS® version 15.0 (SPSS, Chicago, IL, US). Categorical or ordinal data were compared using chi-squared tests and Kendall tau-b respectively. Normally distributed data were compared using independent two-sided t-tests. Skewed data were either transformed logarithmically or analysed non-parametrically (Mann-Whitney U test).

Results

Of 198 patients identified as having undergone aortic surgery, 9 were excluded due to intraoperative/early postoperative death ($n=5$) and missing records ($n=4$). The remaining 189 cases were categorised into two groups: low dose enoxaparin ($n=93$) and high dose enoxaparin ($n=96$) (Fig 1). The groups were comparable for mean age (low dose: 58 years, standard deviation [SD] 16 years; high dose: 59 years, SD 16 years; $p=0.67$), mean cardiopulmonary bypass time (low dose: 157 mins, SD 54 mins; high dose: 171 mins, SD 70 mins; $p=0.13$) and mean aortic cross-clamp time (low dose: 107 mins, SD 37 mins; high dose: 108 mins, SD 39 mins; $p=0.86$). There was no difference in postoperative warfarin (44% vs 45%, $p=0.92$) or antiplatelet therapy (69% vs 56%, $p=0.08$) rates (Table 1).

In-hospital (18% vs 17%), early (≤ 30 days following discharge) (1% vs 2%) and late (>30 days to 1 year) (0% vs 1%) readmission rates for pericardial effusions were similar for low and high dose groups respectively. Total cases of pericardial effusion up to one year were also comparable (low dose 19% vs high dose 21%). The majority of pericardial effusions were managed conservatively (low dose 14% vs high dose 15%) compared with ultrasonography guided drainage (low dose 2% vs high dose 2%) and open surgery (low dose 3% vs high dose 2%) (Table 2).

Three deaths were recorded in the first thirty days postoperatively, all in the high dose group. One further patient, also from the high dose group, was readmitted and died subsequently at 9 months (Table 3). The postoperative course of the four deaths at one year in the high dose group was not significantly higher than the low dose group ($p=0.12$). These cases were reviewed by a study committee to ascertain whether death was attributable to increased enoxaparin dose. However, in none of the deaths was this found to be the case. The types of surgery performed

between the two groups were comparable ($p=0.41$) (Table 4), as was 'redo' surgery (low dose: 8 (9%), high dose: 5 (5%); $p=0.40$) and additional procedures (low dose: 13 (14%), high dose: 17 (18%); $p=0.55$).

Discussion

This is the first study to demonstrate that the potential merits of a more aggressive thromboprophylaxis regimen are not overshadowed by an increased incidence of pericardial effusion rates along with its potentially devastating sequelae in patients undergoing proximal aortic surgery. Despite a reasonable cohort size, the study does not totally exclude the possibility of a type 2 error and it is recommended that further research is focused on a larger cohort to better investigate this problem. However, as proximal aortic surgery is associated with a significant incidence of postoperative pericardial effusion, the routine use of non-invasive transthoracic echocardiography is advocated to detect and monitor progression of pericardial effusion in the postoperative period. Recently, preoperative 25mg oral indomethacin three times daily for seven days has been shown to reduce the incidence of pericardial effusion after aortic surgery² and novel strategies such as this should be the focus of future research.

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