Venous thromboembolism after laparoscopic bariatric surgery for morbid obesity: clinical burden and prevention

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CRD summary
The review concluded that venous thromboembolism incidence after laparoscopic bariatric surgery for morbid obesity appeared relatively low with standard regimens for antithrombotic prophylaxis, but the incidence of major bleeding increased with weight-adjusted doses of heparin with no advantage for venous thromboembolism reduction. Limitations of the included evidence and review procedure suggest that the authors’ conclusion should be interpreted with caution.

Authors' objectives
To assess the incidence of venous thromboembolism for antithrombotic prophylaxis after laparoscopic bariatric surgery for morbid obesity; where possible, the efficacy and safety of this treatment was assessed.

Searching
MEDLINE and EMBASE were searched up to March 2011; search terms were reported. Reference lists were checked for additional studies. Only full reports were considered for analysis.

Study selection
Randomised controlled trials (RCTs) and observational studies that specified the regimen for antithrombotic prophylaxis in patients who had undergone laparoscopic bariatric surgery for morbid obesity were eligible for inclusion. Studies were required to report the incidence of postoperative venous thromboembolism (defined as symptomatic or asymptomatic lower limb venous thromboembolism and/or pulmonary embolism). Studies of open surgery, cava filter, plastic surgery, and splenetic or mesenteric thrombosis were excluded.

In included studies, antithrombotic prophylaxis methods included unfractionated heparin and low-molecular weight heparin with or without graduated compression stockings or intermittent pneumatic compression. Drug doses included: standard unfractionated heparin 5000 UI twice/three times daily; low-molecular weight heparin 30mg twice daily or 40mg daily; fixed dose unfractionated heparin 5000 UI twice/three times daily; and fixed-dose low-molecular weight heparin 40mg once/twice daily or 30mg twice daily. Further details were reported in the paper.

The surgical procedure in all studies was gastric bypass; three studies also included patients who had undergone laparoscopic gastric banding. Objective testing for venous thromboembolism screening was performed to confirm clinical suspicion in most studies; the timing of screening mostly occurred at the onset of symptoms.

One author selected potential abstracts from an initial review of titles and abstracts. Two authors independently selected studies for inclusion in the review from this list. Disagreements were resolved by discussion with a third reviewer.

Assessment of study quality
Three authors independently assessed the quality of the included studies. Observational studies were assessed according to a checklist based on recommendations by the Meta-Analysis of Observational Studies in Epidemiological group. The authors did not state how the quality of RCTs would be assessed.

Data extraction
Two authors independently extracted data onto standardised forms. Data was extracted to calculate of the weighted mean incidence (WMI) of venous thromboembolism for different subgroups, or odds ratios (ORs) for the efficacy of antithrombotic prophylaxis, with associated 95% confidence intervals (CIs).

Methods of synthesis
The weighted mean incidence was calculated in different subgroups. Pooled odds ratios were calculated using a fixed-effect and random-effects model to test the efficacy of antithrombotic prophylaxis. An additional analysis was
performed after reassessing the major bleeding events according to criteria suggested by the International Society of Thrombosis and Haemostasis (ISTH). Heterogeneity was evaluated using $\chi^2$ and $I^2$.

Studies were categorised into four groups according to the regimen for antithrombotic prophylaxis. Separate analyses were also performed for high-quality studies.

Publication bias was assessed by inspection of funnel plots.

**Results of the review**

Nineteen studies were eligible for inclusion in the review (7,590 patients, range 41 to 1500) including 12 prospective cohort studies and seven retrospective cohort studies. Enrolment occurred consecutively in thirteen studies. Eight studies reported loss to withdrawal.

**Standard unfractionated or low-molecular weight heparin regimens:** The weighted mean incidence of pulmonary embolism was 0.5% (95% CI 0.2 to 0.9; $I^2=38$%; 12 studies) and of major bleeding was 3.6% (95% CI 0.9 to 7.95; $I^2=95$%; seven studies, 84 events). Evidence of publication bias was found for major bleeding.

When only high-quality studies were considered, the weighted mean incidence of symptomatic or asymptomatic venous thromboembolism was 1.2% (95% CI 0.2 to 2.9; $I^2=69$%; four studies, nine events). No significant between-study heterogeneity was found after the exclusion of a single study that evaluated a higher dose of heparin.

**Fixed-dose unfractionated heparin:** The weighted mean incidence of pulmonary embolism was 0.3% (95% CI 0.1 to 0.6; $I^2=0$%; six studies, six events) and of major bleeding was 1.6% (95% CI 0.7 to 3.0; $I^2=62$%; four studies, 25 events). The weighted mean incidence according to the ISTH classification was 0.9% (95% CI 0.5 to 1.4; $I^2=0$%; four studies, 18 events).

**Fixed-dose low-molecular weight heparin:** The 30-day weighted mean incidence of venous thromboembolism was 0.7% (95% CI 0.1 to 1.7; $I^2=65$%; four studies, seven events), of bleeding complications was 5.2% (95% CI 0.7 to 13.0; $I^2=95$%; four studies, 74 events), and of pulmonary embolism was 0.2% (95% CI 0.05 to 0.4; $I^2=4$%; four studies, four events).

**Weighted adjusted heparin prophylaxis:** The weighted mean incidence of symptomatic venous thromboembolism was 0.6% (95% CI 0.3 to 1.1; $I^2=0$%; four studies, seven events), of major bleeding was 2.0% (95% CI 1.0 to 3.4; $I^2=55$%; four studies, 22 events), and of major bleeding (according to ISTH criteria) was 1.6% (95% CI 0.6 to 2.9; $I^2=60$%; four studies, 17 events).

**Mechanical prophylaxis:** The weighted mean incidence of symptomatic venous thromboembolism was 0.4% (95% CI 0.2 to 0.8; two studies, five events).

Incidence of venous thromboembolism in studies with longer and shorter surgery duration was also reported.

**Authors’ conclusions**

The rate of venous thromboembolism after laparoscopic bariatric surgery appeared to be relatively low with standard regimens for antithrombotic prophylaxis. The incidence of major bleeding appeared to increase with weight-adjusted doses of heparin; there was no advantage for venous thromboembolism reduction.

**CRD commentary**

The review question was supported by defined inclusion and exclusion criteria. Two databases were searched for full reports; no attempt was made to locate unpublished articles. It was not clear whether this search was restricted by language. Steps were undertaken to minimise the likelihood of error and bias in the extraction of data and assessment of study quality, but similar procedures were performed only in the second phase of study selection.

The quality of the studies was assessed using relevant criteria, but individual results were not reported. All the included studies were observational, so were subject to the inherent biases of this design. Incidence of venous thromboembolism and major bleeding was reported for each antithrombotic regimen, but lack of head-to-head comparisons with standard treatment regimens limited interpretation.
Given the limitations of the included evidence and the possibility that some studies may have been missed, these results should be interpreted with caution.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implication for practice.

**Research:** The authors highlighted the need for RCTs with time-scheduled screening for venous thromboembolism and standardised criteria

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