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Inside

REVIEW

Filters and Heparins in Bariatric Surgery: What's the Verdict?

by AMIR MEHRAN, MD, and TAYLOR RUGGIERO

INTRODUCTION

Venous thromboembolism (VTE) remains one of the most feared complications of bariatric surgery. The incidence of VTE ranges between 0.3 and 2.0 percent with up to 30 percent of incidences resulting in a fatal outcome.[1] Whereas some general agreement exists regarding the benefits of VTE prophylaxis in patients with morbid obesity through early ambulation and the use of sequential compressive devices, little agreement exists regarding other prophylactic measures, such as chemoprophylaxis and inferior vena cava (IVC) filters.

The 2007 American Society for Metabolic and Bariatric Surgery (ASMBS) position statement provided an overview of this topic but did not delve into concrete guidelines.[1] Furthermore, most bariatric surgeons follow their own established patterns and are unlikely to change their current practices in the absence of any demonstrable benefit to doing so. Cognizant that a thorough discussion would possibly require a dedicated consensus conference, we limit our article to the use of low molecular weight (LMWH) versus unfractionated heparin (UFH) and the utility of IVC filters. Since the term *venous thromboembolism* has been liberally applied to both deep venous thrombosis (DVT) and/or pulmonary embolus (PE), our focus will be primarily on the latter more serious complication. The bariatric literature will be reviewed and our program's approach will be described.

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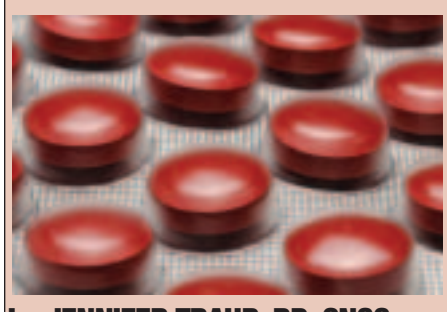
REVIEW

Can Iron Alone Sharpen Iron? Managing Iron Deficiency in the Bariatric Surgery Patient



by JENNIFER TRAUB, RD, CNSC

INTRODUCTION

While there are many challenges in maintaining optimum health status in patients who have undergone bariatric surgery, one issue that remains puzzling for many healthcare professionals is accurately diagnosing and treating iron deficiency. Iron deficiency can present with or without anemia, and its overall incidence is high in the bariatric surgery patient population. Proper diagnosis and management is essential in relieving patient symptoms and preventing long-term consequences associated with iron deficiency, such as impaired memory, physical ability, and mental function.

Bariatric surgery patients are at an increased risk of iron deficiency. The incidence of anemia following bariatric surgery has been reported to be as high as 74 percent and has been mostly ascribed to iron deficiency.[2] There are three major factors that contribute to the increased risk in this patient population. First, surgical bypass procedures reduce absorptive surface area by the exclusion of the duodenum and proximal jejunum, which are the physiological sites of iron absorption.

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ASK THE EXPERTS

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Filters and Heparins in Bariatric Surgery: What's the Verdict?

by AMIR MEHRAN, MD, and TAYLOR RUGGIERO [[[AUT: Please provide degrees, if any, for Ruggiero.]]]

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ABSTRACT
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KEY WORDS
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WHICH HEPARIN, IF ANY AT ALL?

The 2007 ASMBS position statement and the 2008 American College of Chest Physicians (ACCP) guidelines support the use of chemoprophylaxis during bariatric surgery should no medical contraindications to its use exist.[1,4] In a recent survey of the ASMBS membership, some form of heparin was indeed utilized by 95 percent of bariatric surgeons with the majority preferring LMWH over UFH.[2]

In theory, LMWH provides VTE prophylaxis with a reduced incidence of bleeding and heparin-induced thrombocytopenia (HIT). The chief action of LMWH is through its inhibitory activity against both factor Xa (FXa) and thrombin. This is in contrast to UFH. UFH has to bind to both thrombin and antithrombin, which requires a larger molecular structure. Therefore, LMWH has a greater activity against FXa, hence, its enhanced effects and improved safety profile.[5]

In a review of a large medical inpatient database comparing the use of enoxaparin versus UFH, McGarry et al[7] found a reduced rate of VTE in the former group (1.7% vs. 6.3%) with similar hospital costs, incidence of bleeding, and HIT. In contrast, however, Arnold et al[8] at the University of Tennessee found no differences in the incidence of VTE or bleeding in 476 trauma patients who had received either LMWH or UFH. A substantial cost savings was noticed with the use of UFH versus LMWH.

Kothari et al[3] reviewed their experience with the use of enoxaparin (40mg sq two times per day [BID]) versus UFH (5000u sq three times per day [TID]) in 476 bariatric patients split evenly between the two groups. Both regimens were found to be effective in preventing clinically significant VTE with zero incidence; however, the incidence of bleeding and transfusion requirement was higher in the enoxaparin group (5.9% vs. 1.3%), with 1.7 percent of patients requiring a reoperation for bleeding complications. Therefore, enoxaparin use was not recommended.

Escalante-Tattersfield et al[6] described a combination of both types of chemoprophylaxis. In a study of 618 consecutive bariatric surgery patients, UFH (5000 IU every 8 hours) was used in the first 24 hours followed by enoxaparin (40mg every 12 hours) up to the time of discharge. All patients underwent a lower extremity ultrasound at 24 hours to confirm the absence of venous thrombosis. In this group of patients, DVT, VTE, and bleeding were observed in 1, 0, and 10 patients, respectively. Lowering the possibility of postoperative hemorrhage was described as the rationale for this combination therapy.

In a thorough discussion of special populations, Lim[9] discussed the nuances of LMWH use in patients with obesity. Subcutaneous LMWH has a higher bioavailability in plasma and nonfat tissues than in adipose mass. Concerns over bleeding from overdosing LMWH in patients with obesity, therefore, can lead to an inadequate VTE prophylaxis regimen. As a result, a consensus on the appropriate dosing of LMWHs in bariatric surgery does not exist. Various programs have adopted formulas based on body mass index (BMI), adjusted body weights, FXa activity levels, higher fixed doses, or other random variations of standard VTE chemoprophylactic dosing in the nonobese population.

In a prospective, randomized trial, Kalfarentzos et al[10] subjected 60 gastric bypass patients to a daily subcutaneous dose of either 5700 IU or 9500 IU of nadroparin, a LMWH available in Europe. All patients had Doppler studies of their lower extremities preoperatively and at several points postoperatively. No VTE episodes or differences in coagulation parameters were observed in either group. Hemorrhagic complications, however, were observed in two patients in the 9500 IU group versus zero in the 5700 IU group, supporting the use of the lower dose LMWH.

In contrast, Scholten et al[11] came to an opposite conclusion in their nonrandomized study of 481 patients. Enoxaparin 30mg BID was prescribed to the first 92 patients versus 40mg BID in the later group. The two groups were matched except for longer operating room times in the 30mg group. With similar bleeding rates, the incidence of VTE was higher in the former group, which led the authors to recommend the higher dose regimen.

Monitoring anti factor-Xa (aFXa) activity has been suggested as an alternative to fixed-dose LMWH regimens in bariatric surgery. In the nonbariatric patient population, this approach has been advocated in patients with renal insufficiency since LMWHs are cleared via the kidneys. However, no concrete correlation has been clearly demonstrated in the medical literature between aFXa and LMWH clinical efficacy or bleeding risk.[9]

In 102 gastric bypass patients, Paige et al[12] used a BMI-based LMWH regimen (1mg/BMI unit BID) given with particular attention to timing versus surgery start time. In most patients, aFXa levels were also obtained at various postoperative intervals. They reported a 12-percent transfusion rate and no correlation between bleeding and aFXa levels. They concluded that a better dosing system may need to be devised.

Using a fixed dose LMWH approach, Borkgren et al,[13] prospectively studied 223 Roux-en-Y gastric bypass (RYGB) patients who received either 40 or 60mg of enoxaparin BID and continued for 10 days after discharge. Patients with BMI greater than 50kg/m^2 were assigned to the latter group. Anti-factor Xa levels were measured serially, and dosing adjustments were made if levels exceeded established parameters. Clinical suspicion of VTE was entertained in 7.6 percent of the subjects but only one patient in the 40mg cohort was diagnosed with this complication. Five patients (2.2%) developed significant bleeding, all but one patient in the 40mg group. Similar to the findings in the Paige study, the authors found that higher aFXa levels did not correlate with postoperative hemorrhage.

Extended post discharge VTE prophylaxis using warfarin or LMWH has been promoted by some authors. Steinberg et al[14] reviewed 308 consecutive RYGB patients and their experience with the use of enoxaparin. 118 patients received enoxaparin 30mg BID as an inpatient-only regimen versus extended use of the same dosage in 159 patients. All patients underwent lower-extremity venous

ultrasounds prior to discharge. The groups were matched except for a higher bleeding and open conversion rate in the inpatient-only cohort. Defining VTE as either DVT or PE, six VTEs were discovered with four in the inpatient-only group and after discharge; all of whom had had negative lower-extremity ultrasounds previously. Extended LMWH use was therefore advocated; however, the two groups were not matched for VTE risks. Both groups had a higher than average rate of smokers, and the operative times were longer than the other studies reviewed in this article. Although the significance of these findings is unknown, the authors did question the reliability of deep venous duplex ultrasounds in the setting of morbid obesity, a concern brought up by others as well.

Magee et al[15] support the use of extended-term chemoprophylaxis as well. In 735 bariatric patients, dalteparin was utilized perioperatively and up to three weeks after surgery depending on the procedure performed. The daily dosing was adjusted from 2500 IU before surgery to 5000 IU afterwards. In contrast to most programs, however, pneumatic compression devices were not used. With a minimum of six months follow up, symptomatic VTEs were absent and bleeding was recognized in only three patients. The authors, however, did not provide a comparative group of patients in whom LMWH was only used in the immediate perioperative period.

Finally, for patients with HIT, the use of alternative nonheparin anticoagulants, such as fondaparinux, hirudin, or argratroban, have been discussed in the surgical literature. However, there are currently no data related to their use in bariatric surgery, let alone any discussions regarding dosing and BMI adjustment

To further cloud the waters, on the opposite side of the spectrum lies the five percent of bariatric surgeons who do not support the routine use of any chemoprophylaxis due to concerns over postoperative bleeding.[2] Reflecting this viewpoint, Clements et al[16] demonstrated a 0.26-percent incidence of clinically significant VTE in their series of 380 gastric bypass patients who did not receive any form of pharmacologic prophylaxis. The authors, however, were quick to emphasize short operative times, early ambulation, and the use of pneumatic compression devices in lieu of heparin use. The same group published similar findings in their follow-up study of 957 patients.[17] Using the exact same nonchemical prophylactic measures, they reported their incidence of clinical VTE and bleeding as 0.1 and 0.73 percent, respectively. Whether or not IVC filters or other adjuncts had been used in higher risk patients was not indicated in either study. Other bariatric surgeons, furthermore, have to exercise caution before applying these findings to their own patient population, as they might not be able to consistently reproduce the necessary conditions required for nonuse of chemoprophylaxis.

The low incidence of VTE and bleeding in the last study compares very favorably with the previous United Kingdom study of an equal group of patients who did receive chemoprophylaxis perioperatively and for several weeks postoperatively. This equal comparison clearly demonstrates the difficulties in providing concrete guidelines beyond those provided in the ASMBS position statement.[1] Bariatric surgeons have therefore relied on individual solutions based on clinical observations or interpretation of underpowered, small studies. In the absence of randomized trials other than Kohthari's,[3] the preferential use of LMWHs versus UFH may be advantageous only in terms of dosing convenience and continuity should patients be discharged home on the same regimen. The cost effectiveness of this approach is unknown. At the authors' institution, depending on the dosing regimen, the cost difference between LMWH and UFH is 5 to 6 fold.

This review found no strong support for the weight or BMI-based use of LMWHs as there appears to be no consistently reproducible correlation to the incidence of VTE or postoperative bleeding. Similarly, routine use of aFXa activity may be more of scientific interest than of clinical relevance. Its continuous monitoring during typically short hospital stays has to be carefully balanced against its associated costs and whether a meaningful alteration of chemoprophylactic measures can be carried out in a timely fashion based on the results. And finally, the efficacy, cost effectiveness, or even type of extended chemoprophylaxis beyond discharge remains unknown in the absence of larger, randomized studies.

IVC FILTERS: TRUE SAVIORS OR JUST PEACE OF MIND?

Similar to VTE chemoprophylaxis, there is no consensus or solid evidence-based guidelines regarding the use of IVC filters in high risk bariatric patients.[1,18] The commonly quoted ACCP guidelines[4] recommends against IVC filter use in trauma patients which, by proxy, has often been extrapolated to bariatric surgery and used for denial purposes by payers and referring managed-care groups. The validity of this comparison remains beyond the scope of this article especially since most of the evidence is based on older data and before the age of retrievable filters.

Most bariatric surgery authorities define patients with past history of VTE and known history of hypercoagulopathy as a higher risk cohort who should have IVC filters placed preoperatively. Other possible "softer" criteria include evidence of significant venous stasis disease, such as severe lower-extremity edema with brawny skin changes and large varicose veins, super morbid obesity, especially with central distribution, pulmonary hypertension, contraindications to chemical prophylaxis, and relative immobility. Using these criteria, up to five percent of bariatric surgery patients may fall into this category.[18–23]

The recent ASMBS survey confirmed that more than 50 percent of the programs do indeed utilize IVC filters in high-risk patients compared to less than 10 percent just one decade ago.[2] In their retrospective review of 2,100 patients, Obeid et al[19] compared high VTE-risk patients who had received various types of IVC filters versus lower-risk subjects who had not received IVC filters. They found no differences between the two groups in the incidence of clinical VTEs. The authors concluded that the filters were effective in lowering the odds of VTE since a higher incidence would have been expected otherwise; however, they did not discuss the IVC filter types or retrieval rates or any complications related to their use. Furthermore, the higher-risk group had also been placed on low-dose warfarin postoperatively, which may have led to the lower-than-expected incidence of DVT or VTE.

The advent of retrievable filters is thought to have played a key role in the increased utilization of IVC filters.[20–24] Concerns with permanent filters have included infection, migration, vascular injury, bleeding, and most importantly IVC thrombosis.[21] However, in a review of long-term outcomes of IVC filter use in 58 open gastric bypass patients, filter-related thrombotic complications were seen in two patients with only one resulting in serious morbidity.[25] In theory, through early retrieval, the newer generation of filters would avoid filter-related thrombotic complications.

In a cohort of higher-risk patients who had retrievable IVC filters placed concurrent with bariatric surgery, Vaziri et al[20] found DVTs, filter thrombosis, and PE in 21, 14, and 0 percent of their patients, respectively. Of importance, all patients received perioperative chemoprophylaxis and compression devices. There were no device-related complications except for one insertion-site thrombosis. Retrieval was not attempted in 28 percent of patients, and the authors did not discuss longer-term outcomes of this group and whether they remained on chronic anticoagulation. Similar findings have been reported by others as well.[21–24] Rare VTEs were only seen after the removal of retrievable filters and none during their use. Furthermore, up to 21 percent of patients were found to have some form of venous thrombosis despite of chemoprophylactic measures and the use of compression devices.[21,24]

Retrievable IVC filters, however, are not complication free. Filter breakage, caval perforation, and retroperitoneal hematoma have been reported with their removal, albeit rarely.[23] Additionally, 4 to 17 percent of these devices are not explanted; and so, long-term outcomes as well as the need for chronic anticoagulation remain uncharted territory.[21,23,24]

UCLA APPROACH

As indicated before, most bariatric surgeons follow established personal patterns and are unlikely to change their current practices in the absence of any demonstrable benefit to doing so. At our institution, two sentinel patient events led to changes in practice patterns. The VTE prophylaxis consisted of unfractionated heparin 5000 IU every eight hours, starting prior to surgery. Sequential compressive devices and early ambulation within 3 to 4 hours after recovery were used routinely. Patients were not screened for VTE before or after surgery except when clinically indicated. IVC filters were placed only in patients with documented VTE history or known hypercoagulopathy. This approach resulted in a bleeding and VTE incidence of 4.5 and 0.1 percent, respectively. A fatal saddle embolus in the 997th patient, however, forced us to revisit our guidelines for IVC filter placement. Similar to the referenced articles, we expanded the criteria to include all other aforementioned "soft" criteria.

A few years after revising our guidelines for IVC filter placeent, a near fatal case of postoperative hemorrhage and the subsequent review of our database alerted us to a higher-than-average rate of bleeding (6.4%) when compared to the published literature. In the absence of any changes to technique or operative equipment, we concluded that our chemoprophylactic regimen had to be revisited. Unable to discern a noticeable clinical difference between LMWHs or UFH in the bariatric literature, we adopted a new policy of utilizing UFH before surgery and restarting it on the first postoperative day should no evidence of bleeding exist. The bleeding rate has consequently dropped by at least 75 percent. Further maturation of the data will be required to determine the need for any further changes.

SO WHAT IS THE VERDICT?

The incidence of VTE appears to be low in the modern bariatric literature, perhaps reflecting major improvements in surgical technique and the perioperative care of these patients. This review of the bariatric surgical literature provides support for the routine use of chemoprophylaxis but not for any particular type, dosing, or duration. In high-risk bariatric

surgery patients, furthermore, the benefits of retrievable IVC filters appear to outweigh the risks. IVC filter use should be routinely considered in this particular group. Large prospective studies are necessary in order to provide solid recommendations. That is very unlikely to occur as by one account, 128,000 patients are required to discern a statistical difference.[19] Whether centralized databases, such as BOLD®, may provide some type of consensus, however, remains to be seen.

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REFERENCES

1. ASMBS Position Statement on Prophylactic Measures to Reduce the Risk of Venous Thromboembolism in Bariatric Surgery Patients. http://www.asmbs.org/Newsite07/resources. June 2007. Accessed November 22, 2010.
2. Barba CA, Harrington C, Loewen M. Status of venous thromboembolism prophylaxis among bariatric surgeons: have we changed our practice during the last decade? *Surg Obes Relat Dis*. 2009;5(3):352–356. Epub 2008 Nov 24.
3. Kothari SN, Lambert PJ, Mathiason MA. A comparison of thromboembolic and bleeding events following laparoscopic gastric bypass in patients treated with prophylactic regimens of unfractionated heparin or enoxaparin. *Am J Surg*. 2007;194(6):709–711.
4. Geerts WH, Bergqvist D, Pineo GF, et al. Prevention of venous thromboembolism: American College of Chest Physicians evidence-based clinical practice guidelines (8th Edition). *Chest*. 2008;133(6 Suppl):381S–453S.
5. Weitz J. Low molecular weight heparins. *N Engl J Med*. 1997;337(10): 688–698.
6. Escalante-Tattersfield T, Tucker O, Fajnwaks P, et al. Incidence of deep venous thrombosis in morbidly obese patients undergoing laparoscopic Roux en Y gastric bypass. *Surg Obes Relat Dis*. 2008;4(2):126–130.
7. McGarry LJ, Stokes ME, Thompson D. Outcomes of thromboprophylaxis with enoxaparin vs. unfractionated heparin in medical inpatients. *Thromb J*. 2006;4:17.
8. Arnold JD, Dart BW, Barker DE, et al. Unfractionated heparin three times a day versus enoxaparin in the prevention of deep venous thrombosis in trauma patients. *Am Surg*. 2010;76(6):563–570.
9. Lim W. Using low molecular weight heparin in special patient populations. *J Thromb Thrombolysis*. 2010;29(2):233–240.
10. Kalfarentzos F, Stavropoulou F, Yarmenitis S, et al. Prophylaxis of venous thromboembolism using two different doses of low molecular weight heparin (Nadroparin) in bariatric surgery: a prospective randomized trial. *Obes Surg*. 2001;11(6):670–676.
11. Scholten DJ, Hoedema RM, Scholten SE. A comparison of two different prophylactic dose regimens of low molecular weight heparin in bariatric surgery. *Obes Surg*. 2002;12(1):19–24.
12. Paige JT, Gouda BP, Gaitor-Stampley V, et al. No correlation between anti-factor Xa levels, low molecular weight heparin, and bleeding after gastric bypass. *Surg Obes Relat Dis*. 2007;3(4):469–475. Epub 2007 Jun 12.
13. Borkgren-Okonek MJ, Hart RW, Pantano JE, et al. Enoxaparin thromboprophylaxis in gastric bypass patients: extended duration, dose stratification, and antifactor Xa activity. *Surg Obes Relat Dis*. 2008;4(5):625–631. Epub 2008 Feb 8.
14. Raftopoulos I, Martindale C, Cronin A, Steinberg J. The effect of extended post-discharge chemical thromboprophylaxis on venous thromboembolism rates after bariatric surgery: a prospective comparison trial. *Surg Endosc*. 2008;22(11):2384–2391. Epub 2008 Jul 12.
15. Magee CJ, Barry J, Javed S, et al. Extended thromboprophylaxis reduces incidence of postoperative venous thromboembolism in laparoscopic bariatric surgery. *Surg Obes Relat Dis*. 2010;6(3):322–325. Epub 2010 Mar 10.
16. Gonzalez QH, Tishler DS, Plata-Munoz JJ, et al. Incidence of clinically evident deep venous thrombosis after laparoscopic Roux en Y gastric bypass. *Surg Endosc*. 2004;18(7):1082–1084. Epub 2004 May 27.
17. Clements RH, Yellumahanthi K, Ballem N, et al. Pharmacologic prophylaxis against venous thromboembolic complications is not mandatory for all laparoscopic Roux en-Y gastric bypass procedures. *J Am Coll Surg*. 2009;208(5):917–921; discussion 921–923.
18. Rajasekhar A, Crowther MA. ASH evidence-based guidelines: What is the role of inferior vena cava filters in the perioperative prevention of venous thromboembolism in bariatric surgery patients? *Hematology Am Soc Hematol Educ Program*. 2009:302–304.
19. Obeid FN, Bowling WM, Fike JS, Durant JA. Efficacy of prophylactic inferior vena cava filter placement in bariatric surgery. *Surg Obes Relat Dis*. 2007;3(6):606–608; discussion 609–610. Epub 2007 Oct 23.
20. Vaziri K, Bhanot P, Hungness ES, et al. Retrievable inferior vena cava filters in high-risk patients undergoing bariatric surgery. *Surg Endosc*. 2009;23(10):2203–2207. Epub 2009 Jan 28.
21. Schuster R, Hagedorn JC, Curet MJ, Morton JM. Retrievable inferior vena cava filters may be safely applied in gastric bypass surgery. *Surg Endosc*. 2007;21(12):2277–2279. Epub 2007 Apr 13.
22. Trigilio-Black CM, Ringley CD, McBride CL, et al. Inferior vena cava filter placement for pulmonary embolism risk reduction in super morbidly obese undergoing bariatric surgery. *Surg Obes Relat Dis*. 2007;3(4):461–464. Epub 2007 Jun 4.
23. Halmi D, Kolesnikov E. Preoperative placement of retrievable inferior vena cava filters in bariatric surgery. *Surg Obes Relat Dis*. 2007;3(6):602–605. Epub 2007 Jun 4.
24. Overby DW, Kohn GP, Cahan MA, et al. Risk group targeted inferior vena cava filter placement in gastric bypass patients. *Obes Surg*. 2009;19(4):451–455. Epub 2009 Jan 6.
25. Gargiulo NJ 3rd, O'Connor DJ, Veith FJ, et al. Long-term outcome of inferior vena cava filter placement in patients undergoing gastric bypass. *Ann Vasc Surg*. 2010;24(7):946–949.

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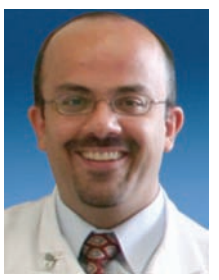

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