



Bari

SPRING MEETING

18 - 19 MAGGIO 2023
THE NICOLAUS HOTEL

CONDIVIDERE PER CRESCERE
Strategie di integrazione
in Chirurgia Bariatrica

Presidente del Congresso
ANTONIO BRAUN

Profilassi multi-modale della Trombosi Venosa Profonda

MIRTO FOLETTO - MICHELE CARRON

AZIENDA-UNIVERSITA' DI PADOVA



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Overview

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Venous thromboembolism: Epidemiology and magnitude of the problem

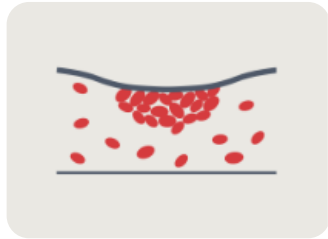
Goldhaber SZ. *Best Pract Res Clin Haematol.* 2012;25(3):235-242.



Among hospitalized medical patients, the 4 risk factors most predictive of VTE in the Intermountain Healthcare database were: (1) previous VTE, (2) **bed rest**, (3) peripherally inserted central venous catheter, and 4) cancer.

VTE: DVT + PE

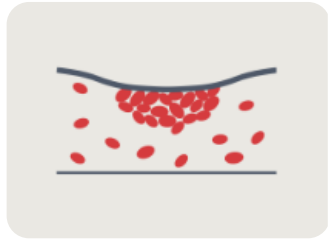
Hospital Acquired Venous Thromboembolism (HA-VTE) - The problem



Venous thromboembolism remains among the **leading causes of preventable hospital death**.¹

Despite it is estimated to be the leading preventable cause of death in hospitalised patients, today hospital acquired venous thromboembolism **(HA-VTE) remains a persistent, preventable and poorly prophylaxed condition** in Europe.^{2,3}

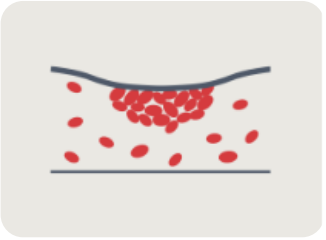

Hospital Acquired Venous Thromboembolism (HA-VTE) - Is Persistent



VTE affects over **1.000.000** Europeans each year, leading to approximately **500.000** premature deaths.^{2, 3} This is more than double of combined deaths due to AIDS (**5.860**), breast cancer (**86.831**), prostate cancer (**63.636**), and transport accidents (**53.599**).^{2,31}

For **1 in 4** patients who experience VTE, **fatal PE** is the first symptom.¹

Hospital Acquired Venous Thromboembolism (HA-VTE) - Is Preventable



Most of VTE cases occurs **within 30 days** of hospitalization, making HA-VTE one of the leading causes of avoidable hospital death.⁴

VTE is a preventable disease and effective prophylaxis is widely available but implementation remains suboptimal.²



Timing of symptomatic venous thromboembolism after surgery: meta-analysis

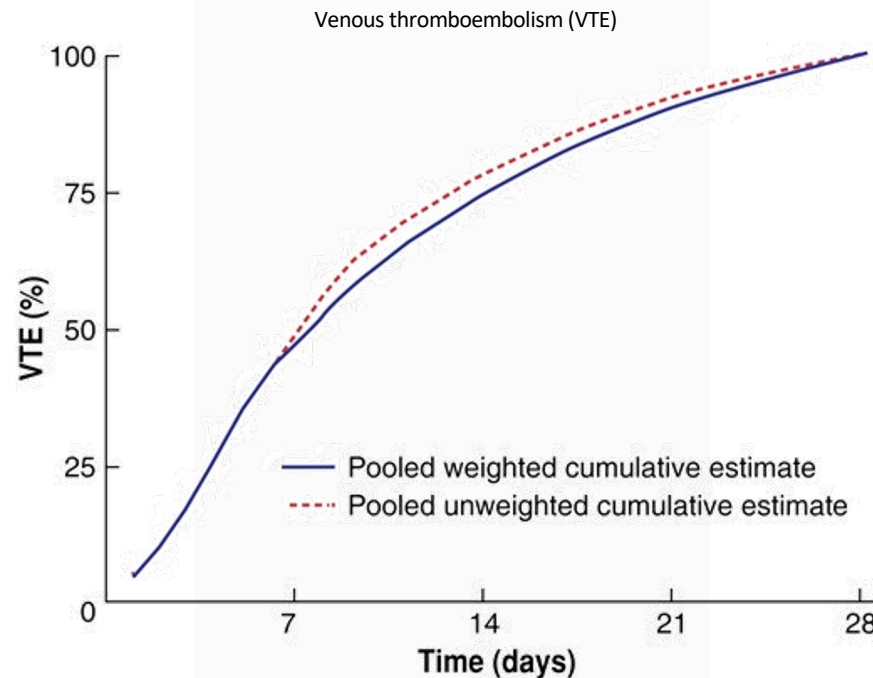
Singh T et al. Br J Surg. 2023;110(5):553-561.

6258 studies were evaluated

22 studies involving postoperative surgical populations were eligible

- 11 general
- 5 urological
- 4 mixed
- 2 orthopaedic

Total **1 864 875 patients** and **24 927 VTE events**.

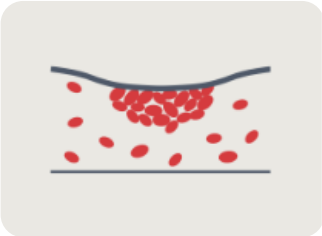



Of blood clots occurring within 4 weeks **after surgery**:

- **47%** occurred by **the first week**
- **74%** occurred by the **second week**
- **90%** occurred by the **third week** after surgery.

Proportion of cumulative occurrence of venous thromboembolism by time during the first 28 days (4 weeks) after surgery: all included studies pooled

Hospital Acquired Venous Thromboembolism (HA-VTE) - Is Poorly Prophylaxed



Only **58%** of surgical and **39%** of medical patients receive the appropriate prophylaxis despite the availability of effective preventive measures.⁵

Public awareness of VTE risk is lower than awareness of the risk of blood pressure, stroke, heart attack and cancer. Only **54%** of people surveyed had awareness of the risk of PE, and only **44%** were aware of the risk of DVT.⁶

Hospital Acquired Venous Thromboembolism (HA-VTE) - Is Costly



Diagnosis and treatment of VTE costs **€3 billion/year** in Europe.^{2,7}

The healthcare cost in patients with VTE can reach **€60K** per year.⁸

Additional LOS from **4.7** (DVT) to **5.4** (PE) days.⁹

Hospital Acquired Venous Thromboembolism (HA-VTE) - Is Costly

Risk assessment **before** admittance (**Caprini's score**):

Choice of prophylactic modality:



Pharmacological

&/or



Intermittent Pneumatic Compression

&/or



Anti-embolism Stockings



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Obese surgical patients

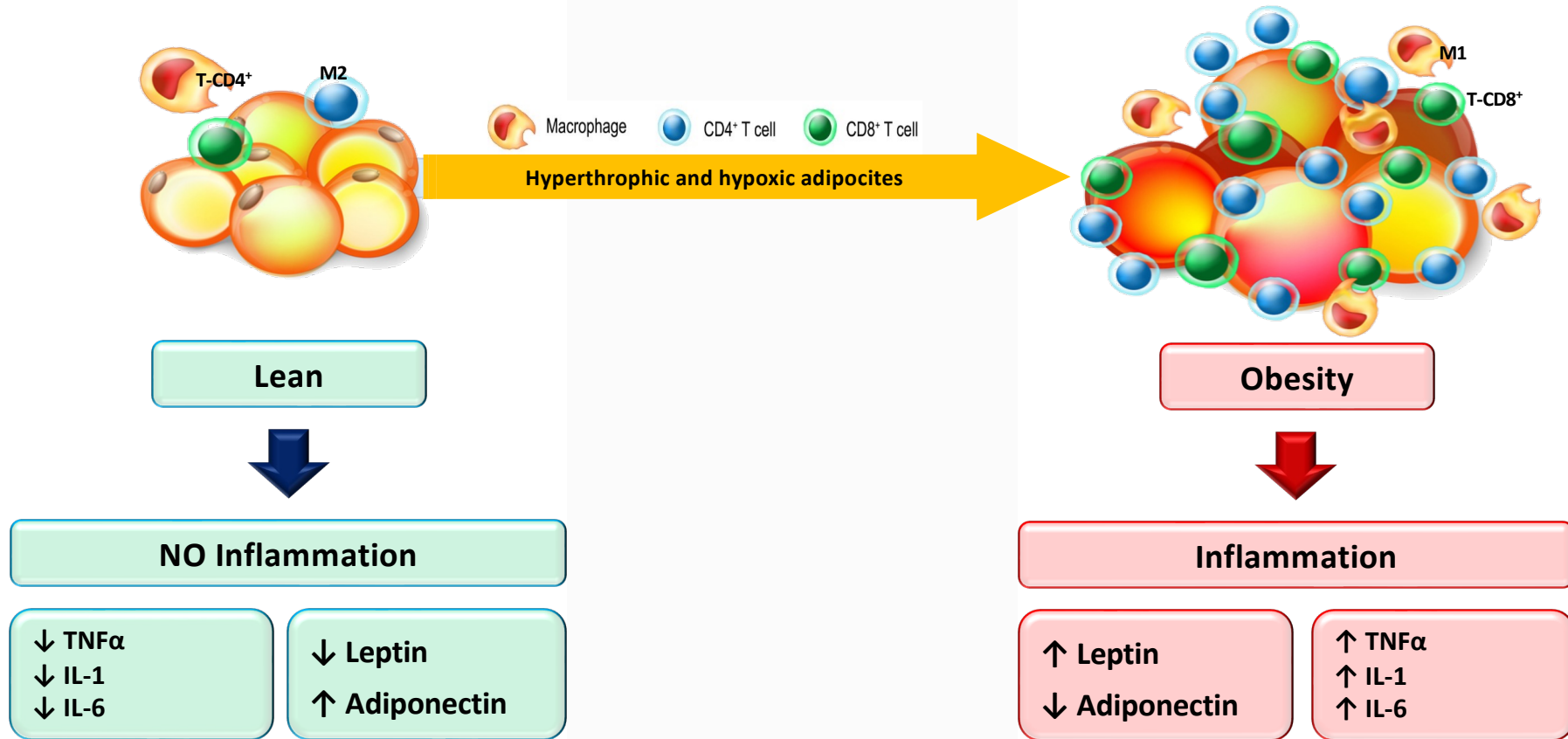
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Obesity and Its Metabolic Complications: The Role of Adipokines and the Relationship between Obesity, Inflammation, Insulin Resistance, Dyslipidemia and Nonalcoholic Fatty Liver Disease

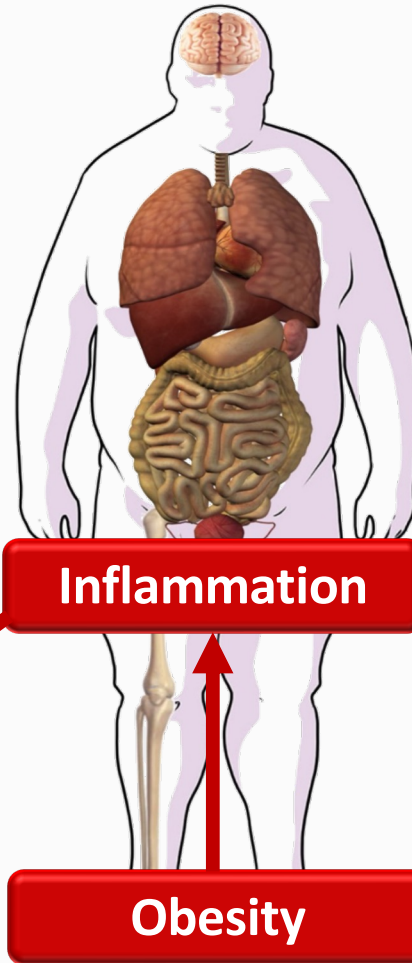
Jung UJ. Int. J. Mol. Sci. 2014, 15, 6184-6223





Perioperative care of the obese patient

Carron M – Foletto M et al. Br J Surg. 2020;107(2):e39–e55



Major depression (OR 1.21)
Bipolar disorder (OR 1.47)
Alzheimer's disease (RR 2.04) - Any dementia (RR 1.64)
Post-operative cognitive dysfunction (RR 1.27)

Hypertention (OR 4.8)
Heart failure (RR 1.90 M - RR 2.12 W)
Ischaemic heart disease (aHR 1.64)
Myocardial infarction (aHR 2.02)
Atrial fibrillation (aHR 1.52 M - aHR 1.46 W)

Diabetes mellitus (aRR 7.28)
Dyslipidemia (aOR 2.2)

Metabolic syndrome
-Stroke (OR 2.16)
-Myocardial infarction (OR 2.01)
-Atrial fibrillation (aHR 1.52 M - aHR 1.46 W)

Hypercoagulability
-Stroke - Myocardial infarction (OR 1.57)
-Deep venous thrombosis (RR 2.50)
-Pulmonary embolism (RR 2.21)

Nonalcoholic steatohepatitis (RR 4.6) - Cirrhosis (RR 4.1)

Renal disease (OR 1.38 Hypertention - OR 1.4 T2D)

Obstructive Sleep Apnoea (OR 6.0 for ↑10% body weight)
-DMV (OR 3.39), DEI (OR 3.46) or both (OR 4.12)
-PO desaturation (OR 2.27)
-PO respiratory failure (OR 2.43)
-PO reintubation (RO 2.05)
-PO cardiac adverse events (OR 2.07)
-PO ICU transfer (OR 2.81)

Obesity Hypoventilation Syndrome
-Cardiac event or cur pulmonare (OR 9)
-PO respiratory failure (OR 10.9)
-PO heart failure (OR 5.4)
-PO prolonged intubation (OR 3.1)
-PO ICU transfer (OR 10.9)

Respiratory disease
-Respiratory complications with severe ↓FEV1 (OR 2.97)
-Cardiovascular complications with severe ↓FEV1 (OR 2.02)

Asthma (RR 2.7)
-PO respiratory complications (OR 2.94)

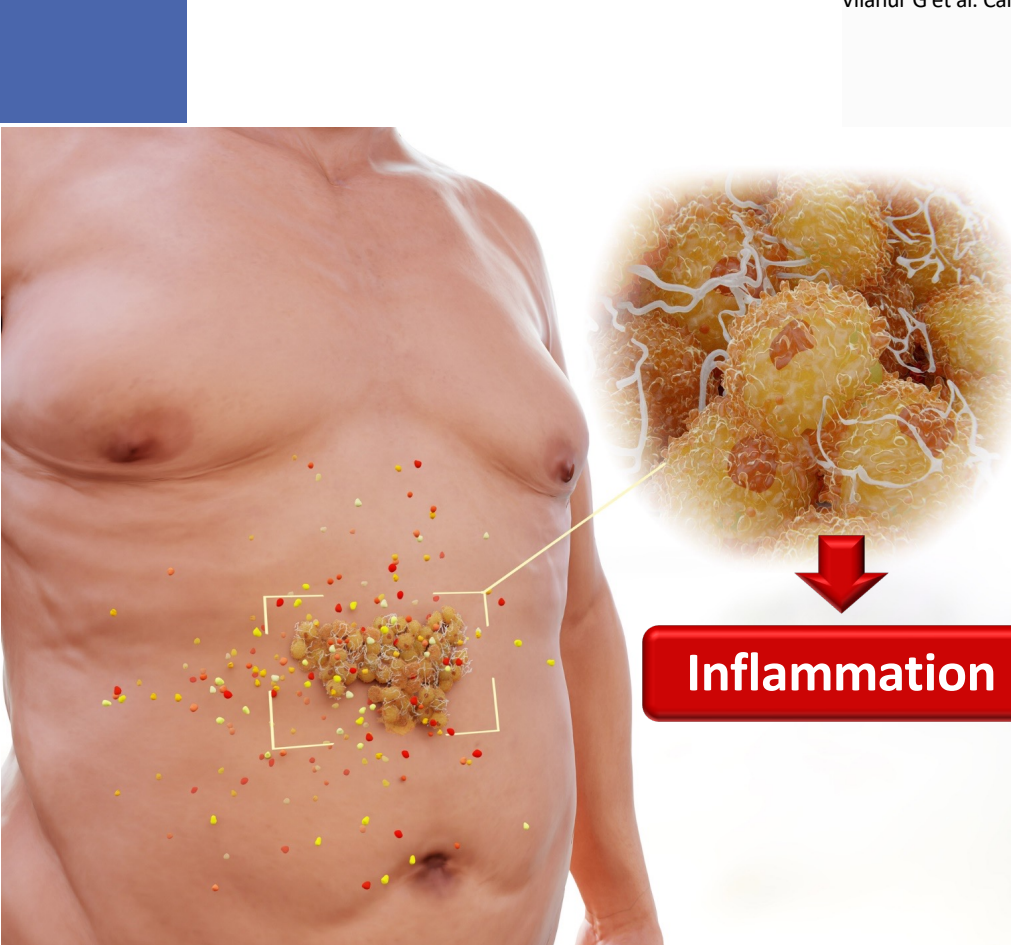
Gastroesophageal reflux disease (OR 1.94)
-PO complications (OR 10.9)

Osteoarthritis (RR 1.12 Hip – RR 1.25 Knee)
Gout (RR 2.67)



New insights into the role of adipose tissue in thrombosis

Vilahr G et al. Cardiovasc Res. 2017;113(9):1046-1054.



- ↑ Leptin
- ↑ TNF α
- ↑ IL-1
- ↑ IL-6
- ↓ PGI $_2$

Endothelial dysfunction

Platelet aggregation
Hyper-reactivity of platelets

- ↑ Tissue Factor
- ↑ Factor VII
- ↑ Factor VIII
- ↑ Fibrinogen

Hypercoagulability

- ↑ PAI1
- ↓ t-PA activity

Impaired fibrinolysis

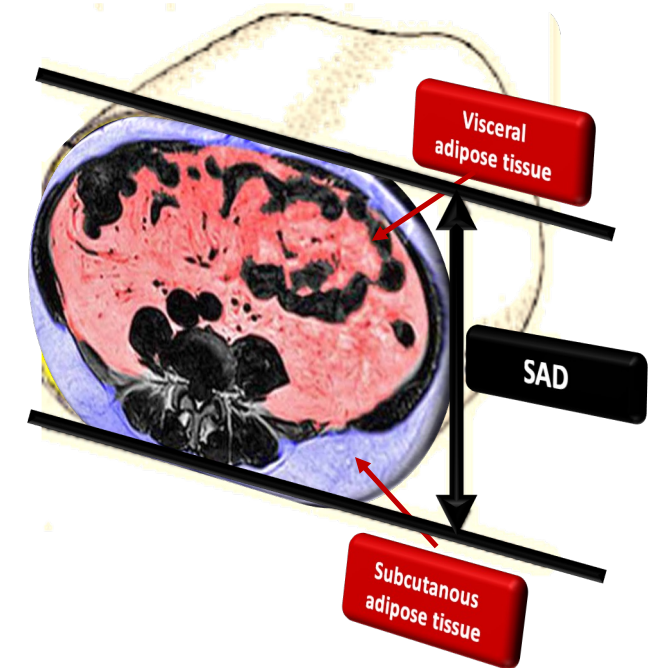
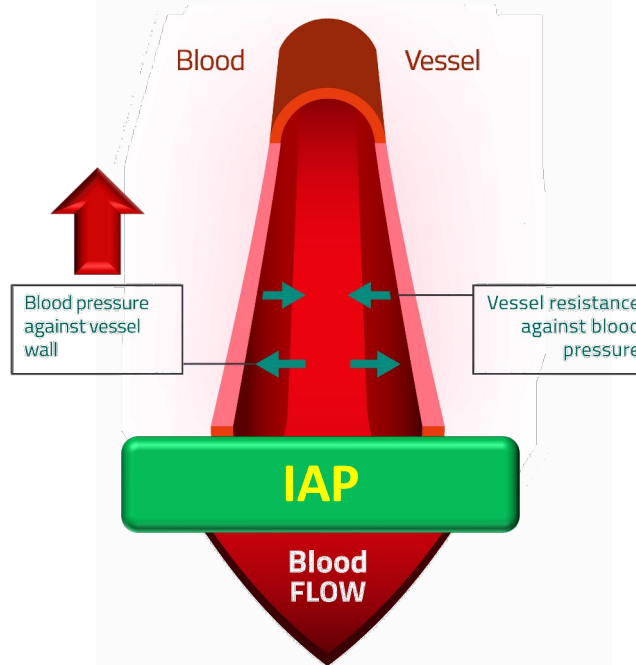
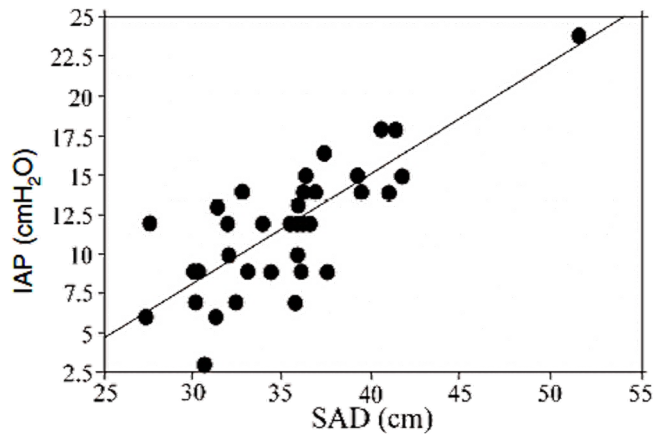
Pro-thrombotic state



Intra-abdominal Pressure in the Morbidly Obese

Lambert DM et al. Obes Surg. 2005;15(9):1225-1232.

Association of **sagittal abdominal diameter (SAD)** and **intra-abdominal pressure (IAP)**

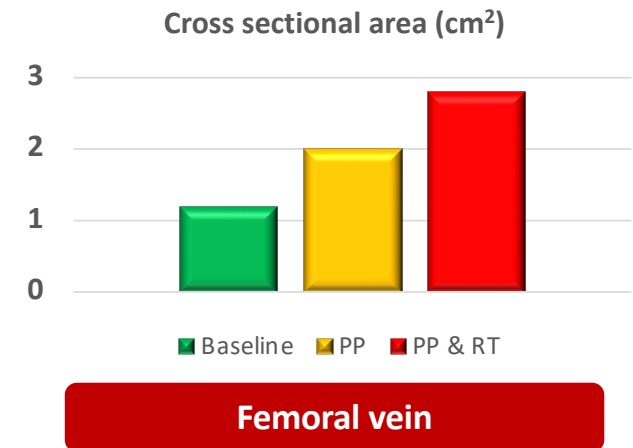
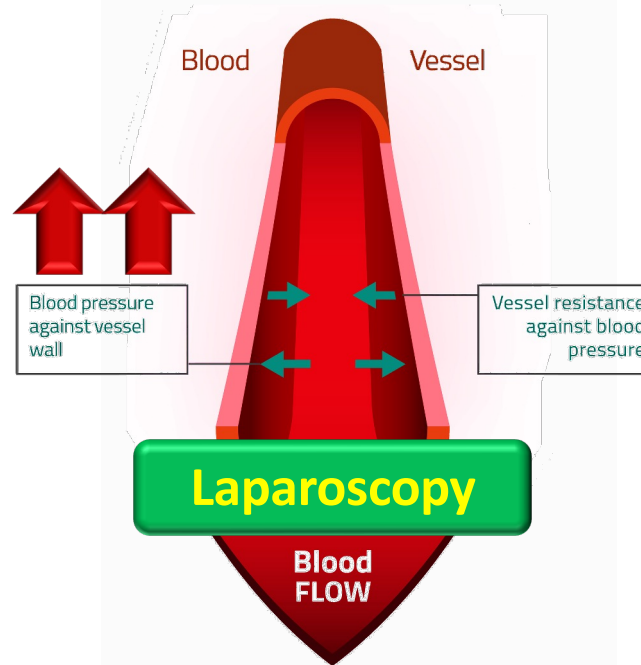
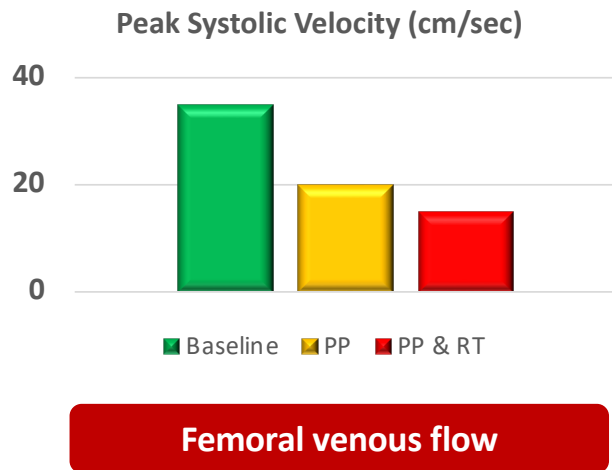


This study clearly demonstrates **elevation in IAP** in morbidly obese subjects.



Duplex ultrasound assessment of femoral venous flow during laparoscopic and open gastric bypass

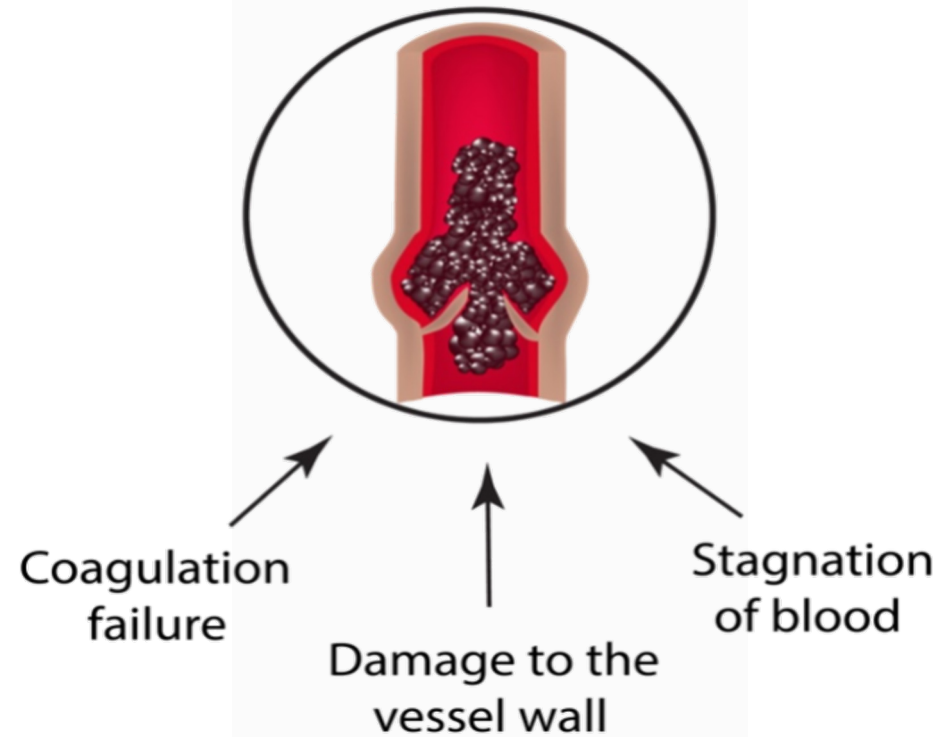
Nguyen NT et al Surg Endosc. 2003;17(2):285-290.

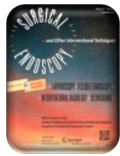


Pneumoperitoneum and **reverse Trendelenburg position** during laparoscopic are **independent factors** for the development of **venous stasis**.

PP: pneumoperitoneum; RT: reverse Trendelenburg

Causes of thrombosis





Enhanced recovery after bariatric surgery: an Italian consensus statement

Marinari G et al Surg Endosc. 2022;36(10):7171-7186.

VTE prophylaxis...

...a teamwork

Preoperative

Intraoperative

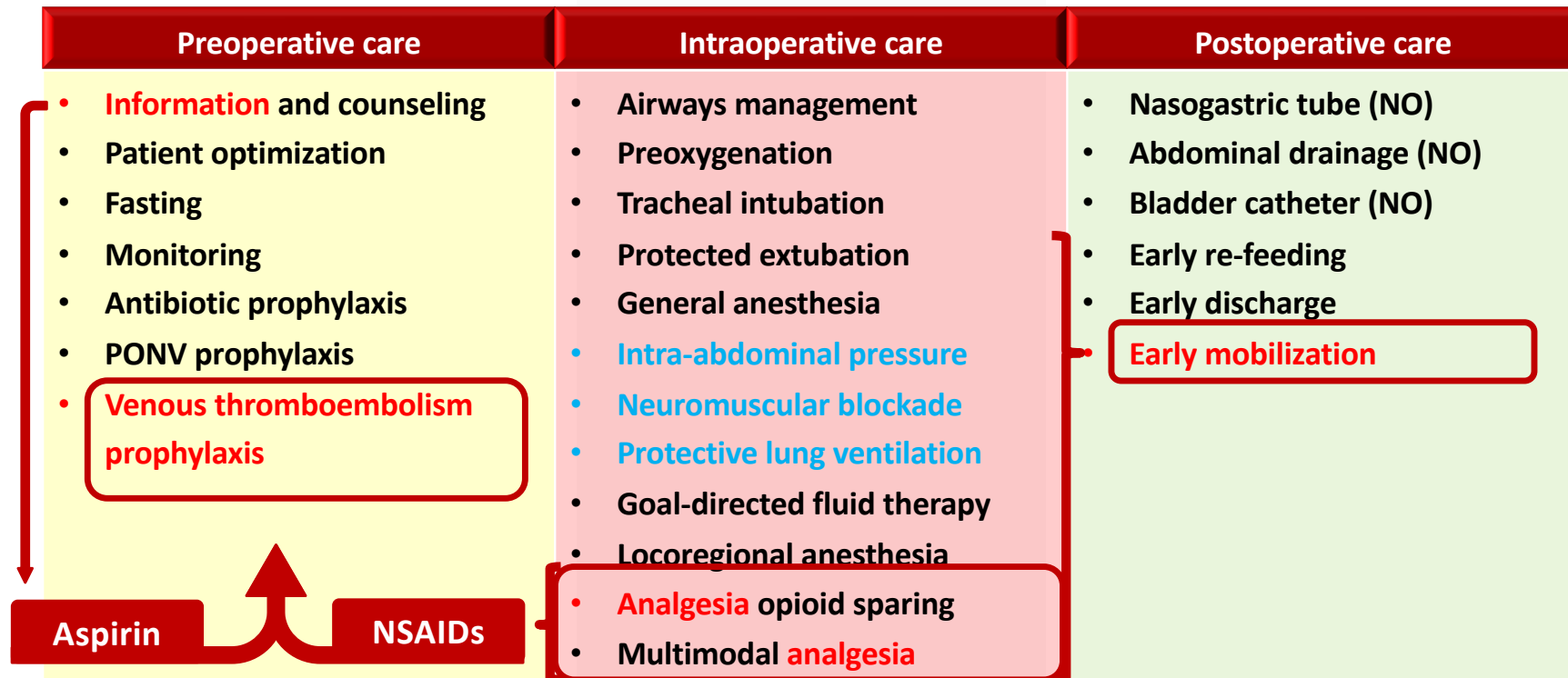
Postoperative



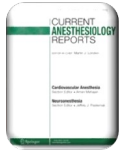


Enhanced recovery after bariatric surgery: an Italian consensus statement

Marinari G et al Surg Endosc. 2022;36(10):7171-7186.



The **recommendations** allow the proper management of obese patients undergoing ERABS **for a better outcome**



Perioperative Guidelines on Antiplatelet and Anticoagulant Agents: 2022 Update

Moster et al. *Curr Anesthesiol Rep* 12, 286–296 (2022).

In **general** population of patients

- **CON:** POISE-2 trial → ↑ major bleeding (HR 1.23)
- **PRO:** Large observational studies (no ↑ major bleeding) and guidelines
Evidence of non inferiority of aspirin to LMWH.¹

In **obese** patients

- VTE after bariatric surgery is approximately 0.1–0.5%.²
- Timing of occurrence (often after discharge).^{2,3}
- LMWH may be not sufficient alone as thromboembolic prophylaxis.⁴

1) O'Toole RV et al. *N Engl J Med*. 2023;388(3):203-213 – 2) Marinari G et al *Surg Endosc*. 2022;36(10):7171-7186 – 3) Singh T et al. *Br J Surg*. 2023;110(5):553-561 – 4) Moaad F et al *Obes Surg*. 2017;27(9):2331-2337



Aspirin or Low-Molecular-Weight Heparin for Thromboprophylaxis after a Fracture

Major Extremity Trauma Research Consortium (METRC), O'Toole RV et al. N Engl J Med. 2023;388(3):203-213.

Pragmatic, multicenter, randomized, non inferiority trial

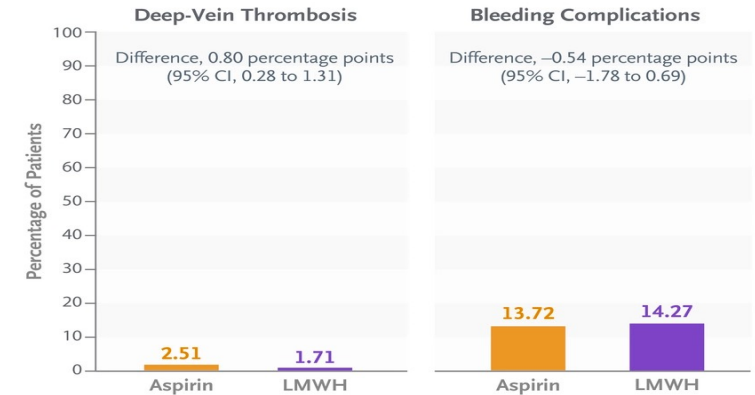
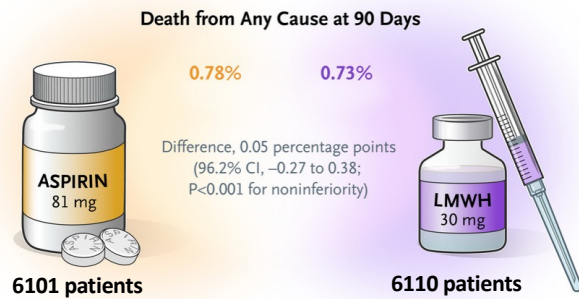
In the hospital: aspirin (81 mg) and LMWH (30 m) twice daily.

After hospital discharge: according to the each hospital protocols

Primary endpoint

Median 21-day of thromboprophylaxis at discharge.

Secondary endpoint



In patients with extremity fractures that had been treated operatively or with any pelvic or acetabular fracture,

thromboprophylaxis with aspirin was noninferior to LMWH



Is LMWH Sufficient for Anticoagulant Prophylaxis in Bariatric Surgery? Prospective Study

Moaad F et al Obes Surg. 2017;27(9):2331-2337.

Coagulation

Within the normal range in the three different time points.

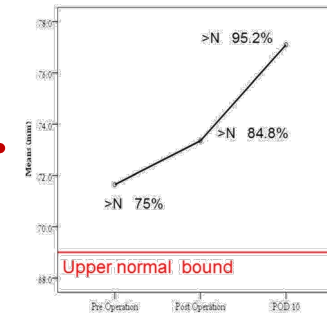
↑ Platelet activity

Pathological values in the three different time points, regardless of the prophylaxis with LMWH

Fibrinolysis

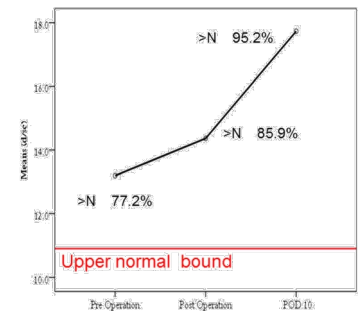
Within the normal range in the three different time points.

Maximal amplitude (MA)



The platelet function of the developed clot

Log derivation of the MA (G)



Clot strength

Ninety-three morbidly obese

TEG to measure coagulation profile

- **Baseline:** before surgery
- **Early:** within 3 h from surgery
- **Late:** within 10-14 days after surgery.

Prophylaxis with **40 mg of LMWH once daily** starting 12 h before surgery and continuing for 4 weeks after surgery

Morbidly obese patients have a strong tendency toward thrombosis.

Prophylaxis at least for 2 weeks after bariatric surgery should be considered - **We recommend adding antiplatelet therapy.**



Guidelines for Perioperative Care in Bariatric Surgery: Enhanced Recovery After Surgery (ERAS) Society Recommendations: A 2021 Update

Stenberg E et al. World J Surg. 2022;46(4):729-751.



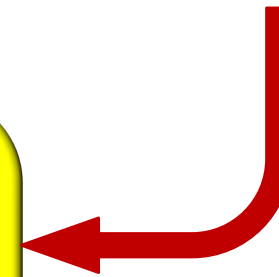
Enhanced recovery after bariatric surgery: an Italian consensus statement

Marinari G et al Surg Endosc. 2022;36(10):7171-7186.

The **ASMBS** guideline suggests **thromboprophylaxis**, including unfractionated heparin or LMWH, given **within 24 h postoperatively**, for all patients after bariatric surgery

A **multimodal venous thromboembolism prophylaxis** via **chemoprophylaxis, mechanical aids, and/or patient mobilization is suggested.**

There is **insufficient evidence** to recommend a **specific dose and duration** of the LMWH treatment.





Venous thromboembolism (VTE) prophylaxis after bariatric surgery: a national survey of MBSAQIP director practices

Giannopoulos S et al. Surg Obes Relat Dis. 2023;S1550-7289(22)00836-X.

- **Both mechanical and chemical VTE prophylaxis: 97.1%:**
- **Chemical VTE prophylaxis**

- 56.5%: enoxiparin

- 32.4%: enoxaparin 40 mg/24 h,
- 22.7%: enoxaparin 40 mg/12 h
- 24.4%: enoxaparin dose adjusted on BMI

Uncertainty

- 38.1 %: heparin

- 46.1%: 5000 units/8 h,
- 22.6%: 5000 units/12 h,
- 20.9%: 5000 units once preoperatively

- **Timing:**

- 81.6%: first dose preoperatively
- 44%: first postoperative dose on the evening of surgery
- 42.2%: first postoperative dose on the next morning.
- 38.7%: extended VTE prophylaxis for 2 weeks
- 28.9%: extended VTE prophylaxis for 4 weeks

264 metabolic/bariatric surgeons

(136 medical directors and 128 ASMBS members)

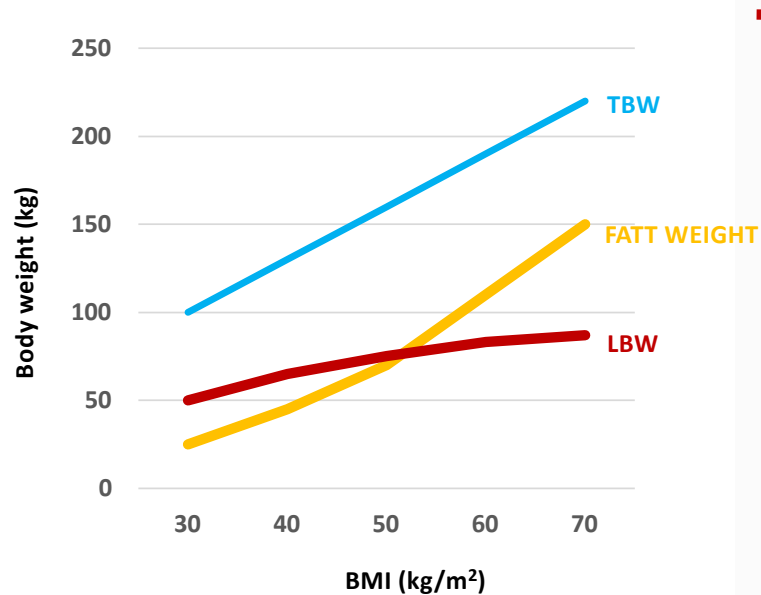


VTE prophylaxis practices vary widely
among metabolic/bariatric surgeons

Drug dosing in obese adults

Barras M, Legg A. Drug dosing in obese adults. Aust Prescr. 2017;40(5):189-193

... **dilemma is enoxaparin, a hydrophilic anticoagulant**. Its licensed dose ... is based on **total body weight**. Many clinicians recognise that this results in **high doses in obesity** and increases the risk of toxicity, so they reduce or **cap the dose** (often at 100 mg) in patients over 100 kg.



NICE do not make any specific recommendations regarding LMWH dosing in obese patients.

A dose based on lean body weight is warranted in this case.

Our experience (Padua): enoxaparin: 0.4-0.8 mg/kg (Lean Body Weight). Max dose: 80 mg daily

EVENT	Higher dose (Enoxaparin 60-80 mg/24 h or 30 mg/12 h)	Standard dose (Enoxaparin 40 mg/24 h)	OR [95%CI]
VTE	0.65% (19/2914)	1.49% (44/2939)	0.47 [0.27-0.82]
Bleeding	5.36% (112/2406)	7.16% (217/3030)	0.86 [0.69-1.08]
EVENT	Reduced dose (Enoxaparin <40 mg/24 h)	Standard dose (Enoxaparin 40 mg/24 h)	OR [95%CI]
VTE	0.38% (2/520)	0.32% (8/2459)	1.14 [0.11-6.84]
Bleeding	0.70% (4/571)	1.31% (34/2579)	0.30 [0.10-0.89]

The **use of LMWH** for anticoagulation **is controversial**. There is the possibility of insufficient anticoagulation with a standard dosage. Moreover, an aggressive dosing strategy will increase the bleeding risk.



Thrombosis and emboli [Phlogose und thrombose imgefässsystem].

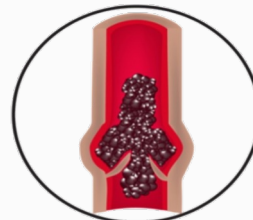
Virchow RL. Gesammelte Adhandlungen zur Wissenschaftlichen Medicine. Frankfurt am Main: von Meidinger & Sohn, 1856:458-636.

Virchow in 1856 suggested that **venous stasis**, **coagulopathy**, and **endothelial injury** are all causes of VTE.



By **treating the different causes** of VTE it is expected that efficacy of DVT prevention would be improved.

Causes of thrombosis



Chemoprophylaxis,



Coagulation failure

Damage to the vessel wall

Stagnation of blood



patient mobilization

mechanical aids



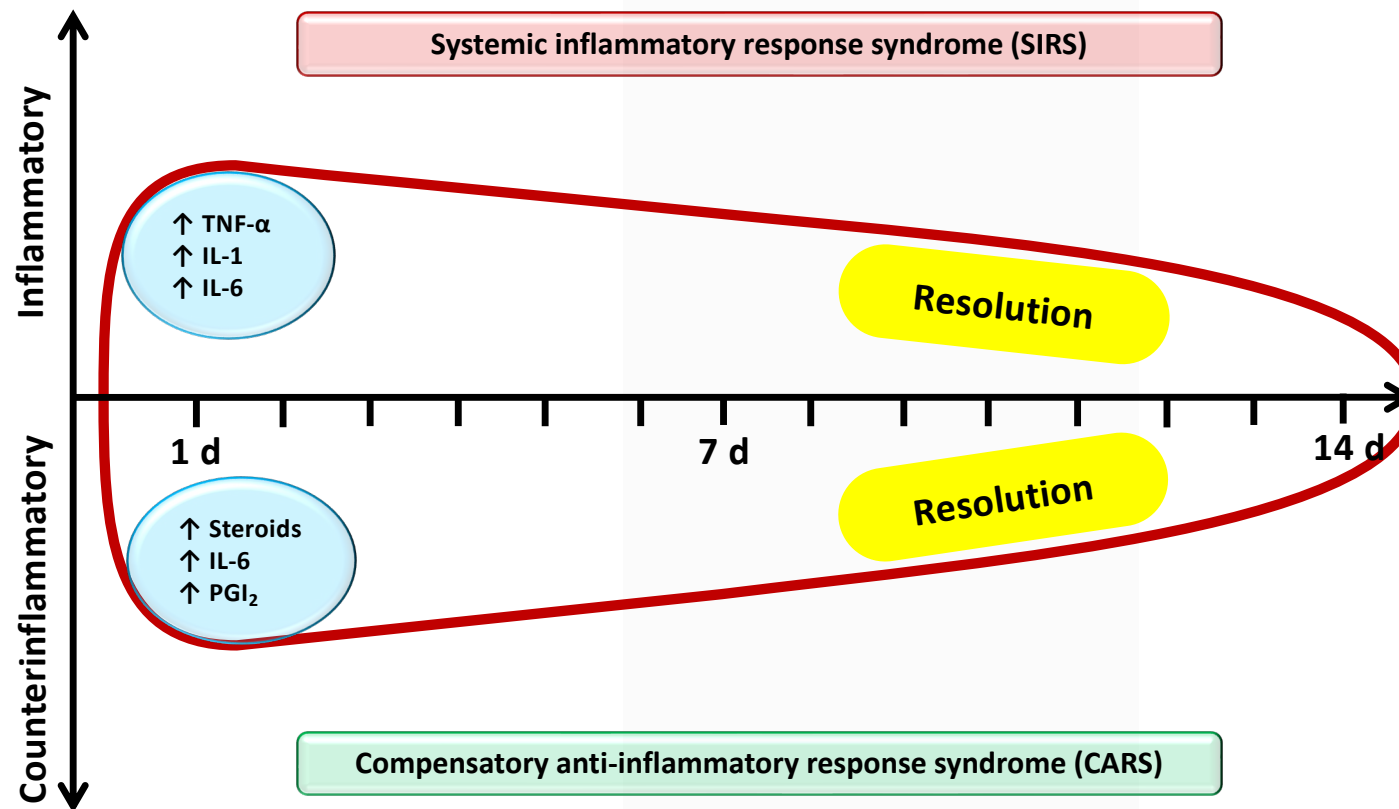
Cell Response to Surgery

Ni Choileain N et al Arch Surg. 2006;141(11):1132-1140.



Changes of Inflammatory Mediators in Obese Patients After Laparoscopic Cholecystectomy

Di Vita G et al. World J Surg. 2010;34(9):2045-2050.



TNF-α and IL-1: non-hepatic manifestations of the acute-phase response, including fever and tachycardia.

IL-6: hepatic component of the acute-phase response resulting in the generation of acute-phase proteins, including C-reactive proteins.

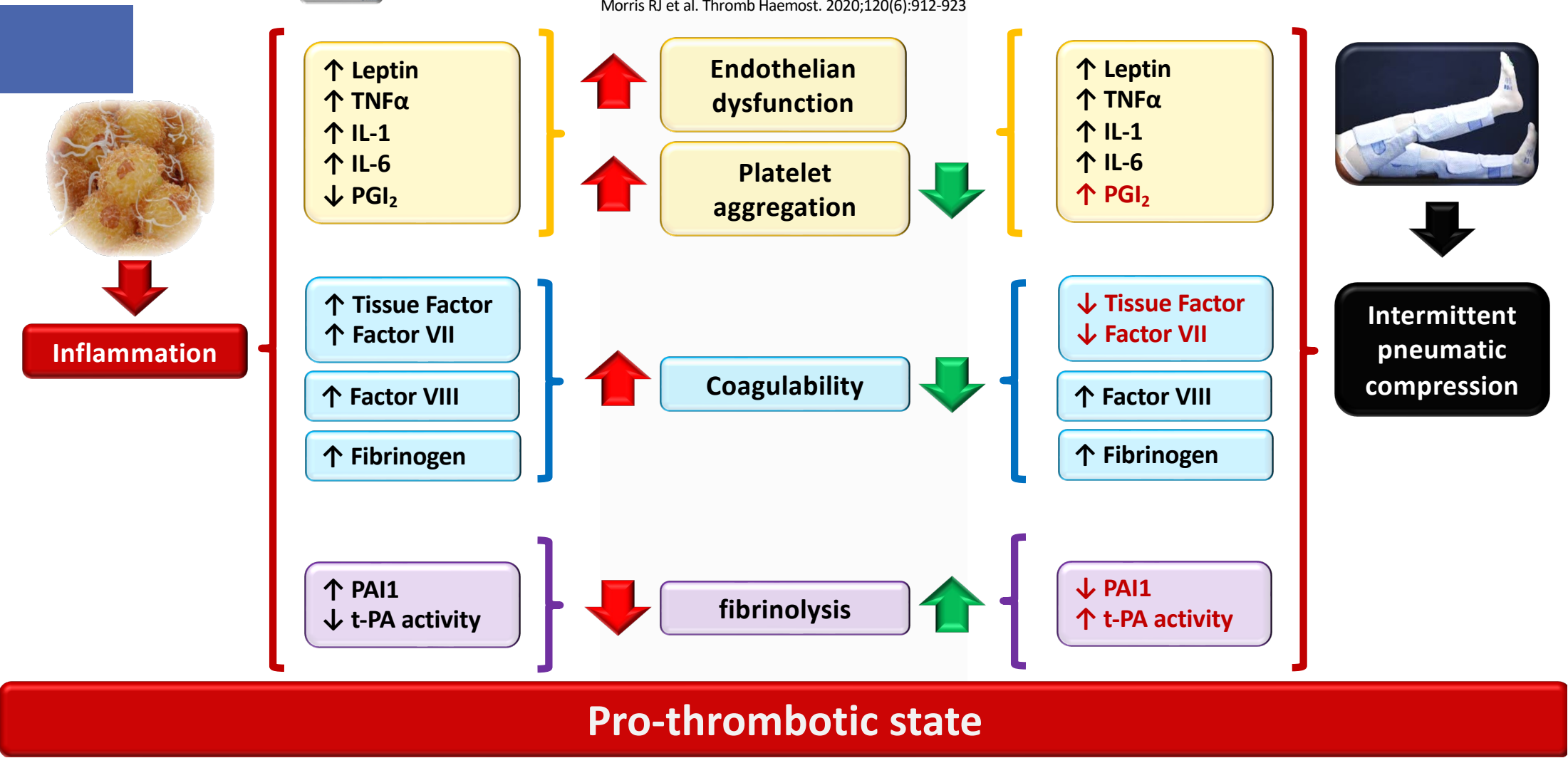
IL-6: attenuating TNF-α and IL-1 activity.

PGI₂: a powerful endogenous immunosuppressant.



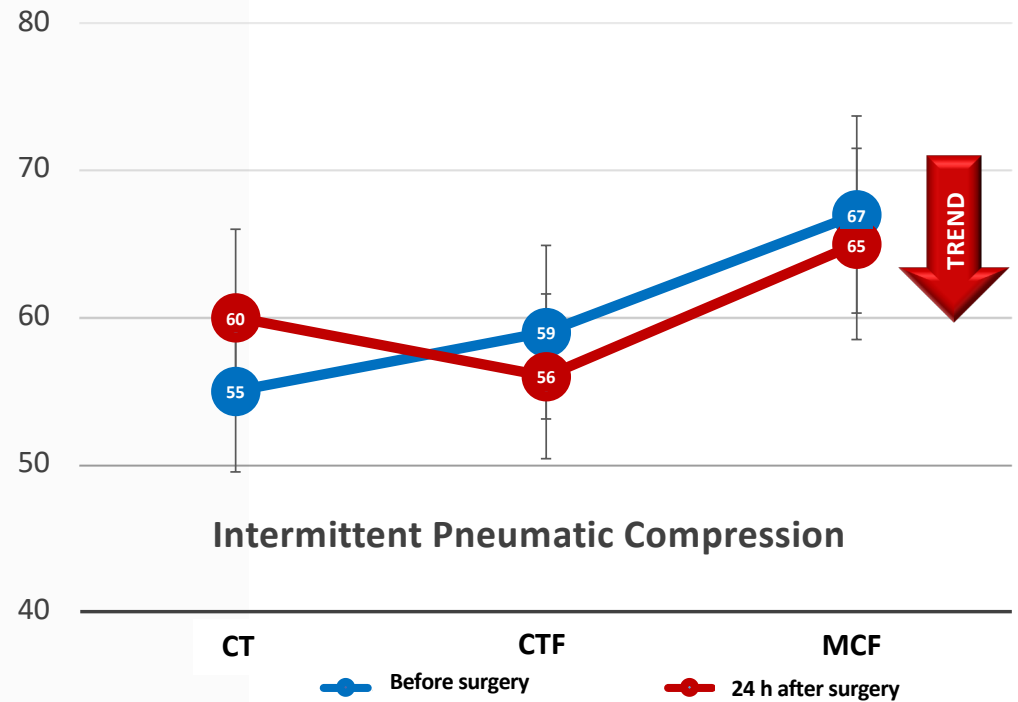
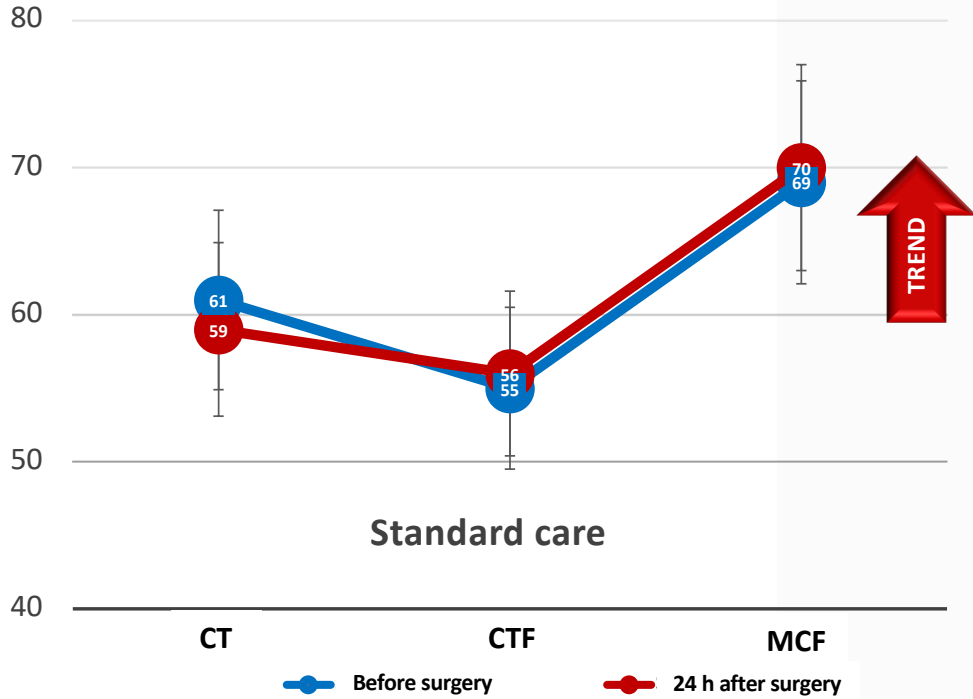
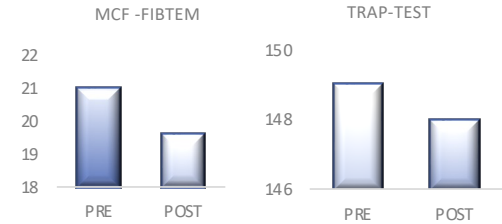
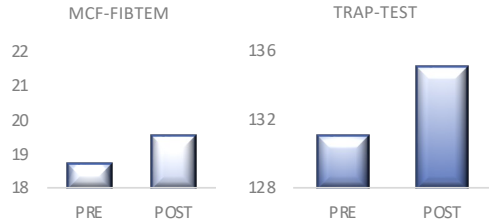
Haematological Effects of Intermittent Pneumatic Compression for Deep Vein Thrombosis Prophylaxis

Morris RJ et al. Thromb Haemost. 2020;120(6):912-923



Our experience

Rotem – EXTEM - FIBTEM



5 Female patients undergoing LSG for each group – Age 43±10 vs. 41±8 (yrs) – BMI 44±2 vs. 45±3 (kg/m²)

EVENT	Intermittent pneumatic leg compression + Pharmacological prophylaxis	Pharmacological prophylaxis	OR [95%CI]
DVT	5.48% (167/3046)	9.28% (288/3105)	0.38 [0.21-0.70]
17 studies 6151 participants			
PE	0.91% (31/3419)	1.84% (61/3318)	0.46 [0.30-0.71]
15 studies 6737 participants			

Combining IPC with pharmacological prophylaxis, compared to pharmacological prophylaxis alone, **reduces** the incidence of both **PE** (low-certainty evidence) and **DVT** (high-certainty evidence).



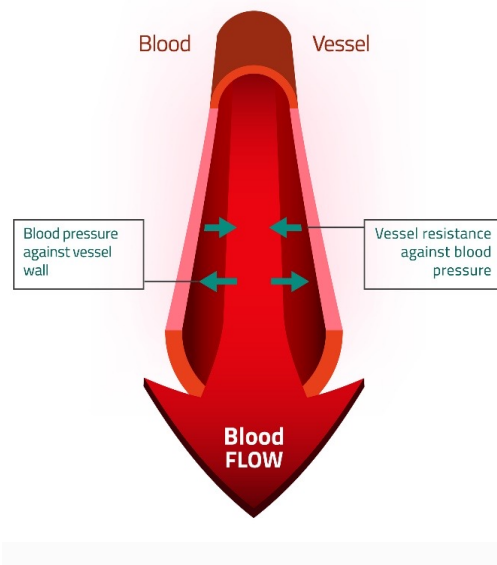
Enhanced recovery after bariatric surgery: an Italian consensus statement

Marinari G et al Surg Endosc. 2022;36(10):7171-7186.

A **multimodal venous thromboembolism prophylaxis**
via **chemoprophylaxis, mechanical aids, and/or patient mobilization**
is suggested.



Thromboembolic stockings



Sequential alternating compressive devices



S.I.C.O.B.
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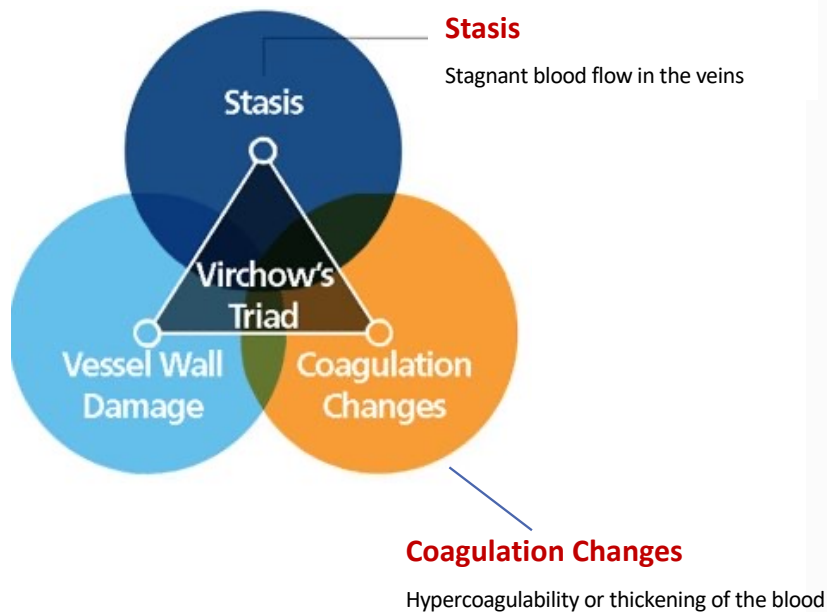
VTE: mechanical prophylaxis

MIRTO FOLETTO

AZIENDA-UNIVERSITA' DI PADOVA

DVT and PE prevention with mechanical prophylaxis

IPC is an effective prophylaxis to reduce DVT and PE risk, as it acts on 2 of 3 factors of Virchow's triad:



1. **Stasis** - Increases blood flow

2. **Vessel wall damage** - micro-tears in the endothelium, such as those caused by venous distention

3. **Blood coagulation changes** - Stimulating fibrinolytic activity

What is Intermittent Pneumatic Compression (IPC)?

Intermittent pneumatic compression (IPC) refers to compressing a patient's leg intermittently by using a controller (pump) to pneumatically inflate a disposable sleeve wrapped around the patient's limb

An IPC system generally consists of three components:

1. Controller
2. Tubing
3. Disposable garments

Which is appropriate Intermittent Pneumatic Compression prophylaxis ?

An effective therapy must **favor the venous return of the lower limbs**, moving as much blood as possible. To do this, the compression must meet these requirements:

1. Circumferential

- Increases fibrinolytic activity
- Quickly empty the femoral veins
- It quickly collapses the femoral cusps where fatal blood clots can form

2. Sequential

- Maximizes blood flow near the femoral veins
- Promotes unidirectional blood flow

3. Gradient

- Reduces the risk of distal blood entrapment

Which is appropriate Intermittent Pneumatic Compression prophylaxis ?

An effective therapy must **favor the venous return of the lower limbs**, moving as much blood as possible. To do this, the compression must meet these requirements:

1. **Circumferential**

- Compression circumferential in that it compresses the entire circumference of the leg- front, back and sides



2. **Sequential**

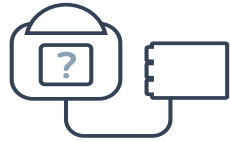
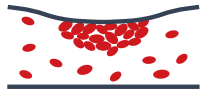
- 3 separate chambers that squeeze the leg



3. **Gradient**

- 3 chambers inflate as a different compression pattern

Mechanical prophylaxis patient benefits



- Safe therapy to prevent deep thrombosis and pulmonary embolism
- Simply to place and use
- Comfortable therapy for patients who appreciated the compression like a massage
- Transpirations, lightness and softness of the sleeve

Real life

In the ward before surgery



Real life

In the OR

Before surgery



After surgery



Real life

In the ward after surgery





S.I.C.O.B.
Bari

SPRING MEETING

**18 - 19 MAGGIO 2023
THE NICOLAUS HOTEL**

CONDIVIDERE PER CRESCERE
Strategie di integrazione
in Chirurgia Bariatrica

Presidente del Congresso
ANTONIO BRAUN

Profilassi multi-modale della Trombosi Venosa Profonda

Thank you for attention

MIRTO FOLETTO - MICHELE CARRON

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