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Are graduated compression stockings still essential for VTE prophylaxis in general surgical patients?*

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Sind Kompressionsstrümpfe zur Thromboseprophylaxe in der Allgemeinchirurgie noch erforderlich?

Les bas à compression élastique dégressive sont-ils essentiels pour la prophylaxie de la maladie thrombo-embolique en chirurgie générale?

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Venous thromboembolism (VTE) continues to account for considerable morbidity, mortality and medical care expense: in the USA the incidence of deep venous thrombosis (DVT) is reported to be approximately 450 000 cases per year and the overall incidence of pulmonary embolism (PE) to be about 355 000 cases per year (8). Numerous studies have indicated that especially surgical and trauma patients are at significant risk for developing venous thromboembolic complications, including pulmonary embolism. Without prophylactic treatment, the risk of VTE (12, 19, 50) is considered to be

- 25–30% in general surgery (8, 13, 46),
- 60% after major trauma (22, 23) and
- up to 45–70% with hip or knee replacements.

Both physical and pharmacological measures aimed at preventing thromboembolic events have been previously evaluated. In earlier studies graduated compression stockings were found to substantially reduce the incidence of VTE in surgical patients (2, 13, 30, 46, 60). During recent years, however, notable developments in pharmacological thromboprophylaxis have been achieved. The introduction of low molecular weight heparins (LMWH), in particular, has resulted in significant advances in treatment modalities so that today they have become the standard for VTE prophylaxis in most countries. The prophylactic properties of LMWHs have yielded equal or even slightly better outcomes than unfractionated heparins. Moreover, they have fewer side effects, do not require laboratory monitoring, and possess pharmacokinetic characteristics which permit their use as a subcutaneously administered, fixed daily dose. LMWHs are reported to reduce the overall incidence of deep vein thrombosis after general surgery by up to 70% (2, 33).

In light of this progress, reevaluation of the concomitant use of graduated compression stockings, as it is still recommended in this setting, is warranted.

Patients, methods

Study population and design

The study population consisted of all patients treated in a general surgery department over a period of four years.

With a prospective observational study design, the incidence of symptomatic deep venous thrombosis and pulmonary embolism was investigated with two different VTE prophylaxis regimens. During the

- first 24 months (group A) patients at risk received combined treatment for the prevention of thromboembolism consisting of LMWH and graduated compression stockings,
- second 24 month period (group B) only LMWH was used for prophylaxis.

Treatment

Prophylactic treatment was given to all patients undergoing major surgery (>30 min). The treatment was initiated the day before surgery and was continued for five days thereafter, or until complete remobilization was achieved. The prophylactic measures were also taken in patients with minor surgery and patients who were not actually operated on if they were expected to be immobile for more than 6 hours during the day for more than two days. Patients under the age of 14 did not receive VTE prophylaxis.

The thigh-length compression stockings (T.E.D.® Kendall) in group A were fitted to each patient's legs according to the manufacturer's instructions. The patients were advised to wear them 24 hours a day. Compliance with the wearing of stockings was checked at least twice daily. Patients found without stockings or not wearing them properly on more than two occasions were categorized as noncompliant. Patients with known significant peripheral artery disease (intermittent claudication and/or ABI <0.7) did not receive stockings.

The LMWH employed in both groups was enoxaparin. It was administered according to a simple weight-adjusted protocol. Patients with a body mass index (BMI) of up to 30 kg/m^2 received 20 mg of enoxaparin and patients with BMI >30 kg/m^2 received 40 mg – subcutaneously, once daily. Patients in whom the use of LMWH was contraindicated (those with a history of or suspected active HIT II or allergic skin reactions) were treated with 15 mg of hirudin subcutaneously, twice daily.

In group B, no stockings were used. The prophylactic treatment consisted of LMWH (or hirudin) alone, administered following the same protocol as in group A.

All patients in groups A and B were strongly encouraged to get out of bed and walk as early as possible.

Outcomes

In all patients with clinical symptoms suggesting deep vein thrombosis colour-Doppler ultrasonography of the pelvic and leg veins was done, including compression testing of the leg veins. The leg examination included all veins from the thigh down to the ankle. All sonographic examinations were carried out by two highly-skilled examiners with an ATL / Philips HDI 3000 machine, using a 3–5 mHz curved array scanner for the pelvic veins and a 5–7 mHz phased array scanner for the leg veins. If this examination was temporarily not possible, or if the results were inconclusive, ascending phlebography followed.

Patients with symptoms of pulmonary embolism underwent spiral computed tomography of the lungs. This was judged positive if it revealed distinct filling defects in large vessels. If the diagnosis remained inconclusive after this examination, a ventilation-perfusion lung scan (judged positive only in cases of „high probability" results) and/or a pulmonary angiography was performed.

Results

A total of 6187 patients (Tab. 1) were treated in the general surgery department during the study period, with a total of 5561 operations.

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Treatment group characteristics

In group A (treated with stockings and LMWH), there were 3181 patients: 1742 men and 1439 women, with a mean age of 48 years. The mean duration of hospital stay was 7.3 days; 2720 of the A patients had surgery with a total of 3050 operations (Tab. 1, Tab. 2). Four hundred sixty-one patients had no surgery. VTE prophylaxis (Tab. 3) was applied to a total of 2623 (82.5%) of the 3181 patients of period A: to 2422 (89.1%) patients with surgery and to 202 (43.8%) patients without surgery. Fifteen patients in group A could not wear compression stockings due to advanced occlusive artery disease and six others because of extreme obesity. Twenty-eight patients were non-compliant with wearing stockings. Three patients in group A needed to be treated with hirudin, instead of LMWH, due to contraindications.

In group B (only LMWH), 2986 patients were treated: 1691 men and 1295 women, with a mean age 49 years. The mean duration of hospital stay was 6.2 days and 2553 patients had a total of 2911 operations. Four hundred thirty-three patients had no surgery. VTE prophylaxis was provided to 2512 (84.0%) of the 2986 patients in period B: to 2305 (90.3%) patients with surgery and to 202 (46.6%) patients without surgery. Two patients had to be treated with hirudin, instead of LMWH.

Tab. 1
Patient characteristics, type of surgery

		group A	group B
		LMWH + stockings	LMWH only
patients	patient number, total	3181	2986
	men	1742	1691
	women	1439	1295
	age (years)	48	49
	days of stay	7.3	6.2
type of surgery	vascular	202	157
	thyroid	149	104
	stomach	119	62
	small intestine	69	85
	appendix conventional	227	155
	appendix lap	99	166
	rectum	270	209
	colon	215	205
	liver	5	4
	gallbladder conventional	44	29
	gallbladder lap	190	186
	pancreas	3	3
	herniotomy conventional	357	381
	herniotomy lap	50	44
	miscellaneous abdominal	82	33
	mastectomy	130	93
	thorax	224	202
	violence (gunshot, knife wounds)	45	29
	skin (tumors, lymphadenectomy)	83	81
	wounds, wound sutures	167	175
	miscellaneous	35	29
	total	3050	2911

Outcomes (Tab. 4)

Deep vein thrombosis

Thirty-eight patients in group A and 40 in group B developed clinical symptoms suggestive of a deep vein thrombosis which required further investigation. Thirty patients in A and 31 patients in B received color-duplex assisted compression sonography and eight patients in A and nine in B received phlebography. A DVT was confirmed in six patients in group A and in three patients in group B.

Tab. 2
Number of operations per patient

number of operations	group A	group B	p-value
	LMWH + stockings	LMWH only	
1	2517	2349	0.659
2	127	124	0.758
3	44	45	0.684
4	18	19	0.596
5	9	9	0.893
6	5	10	0.152
8	0	1	0.302
10	0	1	0.302

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	VTE prophylaxis	group A (LMWH + stockings)	group B (LMWH only)	p value
patients		3181	2986	
with surgery	–	2720	2553	0.992
	+	2429 (89%)	2165 (90.3%)	0.151
without surgery	–	461	433	0.592
	+	232 (50.0%)	202 (46.7%)	0.299
total	+	2673 (82.9%)	2567 (84%)	0.115

–/+: with/without VTE prophylaxis

Tab. 3
VTE prophylaxis

	group A (LMWH + stockings)	group B (LMWH only)	p value
examinations	total/positive	total/positive	
duplex	30/5	31/3	
phlebography	8/1	9/0	
spiral CT	5/1	4/3	
vent.-perf. scan	1/0	0/0	
pulm. angiography	0/0	1/1	
total examinations	44/7	45/6	0.986
patients with VTE	7	5	0.665
event rate	0.22	0.20	0.87

Tab. 4
Examinations and VTE rates

Pulmonary embolism

A pulmonary embolism was suspected in six patients in group A and seven in group B during their hospital stay. 12 of these patients underwent spiral computed tomography of the lungs, one patient had a ventilation-perfusion scan and one needed an additional pulmonary angiogram. The pulmonary embolism was confirmed in one patient in group A and in three in group B.

Characteristics of patients with VTE

All the 12 patients (7 in group A, 5 in group B) with confirmed VTE were receiving prophylaxis at the time the VTE event occurred. The mean duration of hospital stay in these patients was 38 days in group A and 39 days in group B. All patients with PE in both groups had malignant disease.

Discussion

This study, which took place over a period of four years and involved 6167 patients on a general surgery ward, revealed no significant differences in the incidence of symptomatic venous thromboembolism whether graduated compression stockings were used in addition to LMWH prophylaxis, or not.

A review of the literature over the last three decades shows that, despite significant advancements in the prevention of venous thromboembolism, there is still a considerable degree of variation in regard to risk group definitions, the number of patients receiving prophylaxis, and prophylactic modalities.

To achieve better standardization in VTE prophylaxis, several consensus conferences have generated guidelines which are aimed at promoting and attaining adequate VTE prophylaxis for the individual patient. Yet, even the latest guidelines concerning the prevention of thromboembolism in surgical patients, namely the updated ACCP guidelines from 2004 (24) and those of the International Consensus Statement dating from 2006 (46), are not completely concordant. In regard to general surgery patients, the former do not recommend a specific prophylaxis in low-risk patients, propose the alternative use of stockings or heparins in moderate- and higher-risk patients, and recommend combination therapy only in very high-risk patients. The latter consider the use of compression stockings in low risk patients, recommend stockings with intermittent pneumatic compression as an alternative to LMWH in moderate risk patients with bleeding tendency and only consider compression stocking as an adjunct to LMWH in high risk patients. In other fields of surgery (for example urologic surgery or gynecologic surgery) there is even less evidence for the necessity of compression stockings. In these fields the recommendations are either extrapolated from general surgery or comments concerning the use of compression stockings are lacking – as is also the case in all recently published studies on VTE prophylaxis in medical patients (36, 41, 52).

There are generally nine studies cited which substantiate significant VTE risk reduction following the use of graduated compression stockings in general surgery (65). All of them were carried out 10 or more years ago (3, 5, 28, 43, 55, 56, 58, 63, 64). The study designs are rather heterogeneous and most of them included a total of less than 100 patients (5, 28, 55, 56, 58). Only two out of the nine studies (3, 28) compared the use of stockings with the absence of prophylactic measures. These found a 50% reduction in the rate of venous thromboembolism in patients who wore stockings. In the seven other studies, a combination therapy was used consisting of either intermittent pneumatic compression (43, 56) or pharmacological methods (dextran, low dose heparin, dihydroergotamine-heparin) together with graduated compression stockings (5, 43, 58, 63, 64). In five of the studies the effectiveness of compression stockings was investigated on only one of the patient's legs; the other leg served as a control (5, 43, 55, 56, 58).

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Several studies in the following years have provided evidence that low dose heparin significantly reduced the incidence of postoperative VTE, and the benefit appeared to increase with the additional use of compression stockings (11, 15, 31, 32, 45). Subsequently, low dose heparin in combination with compression stockings became the most widely adopted measures for VTE prophylaxis in general surgery – a regimen which has been used in many facilities until today (4, 10, 12, 65).

When LMWHs were introduced into VTE prophylaxis in the mid-1990s, they first proved their effectiveness in orthopedic surgery, namely with hip and knee replacements. Later LMWHs were adopted in general surgery and were combined with the compression stocking prophylaxis already in use. Only four studies can be found which show an advantage to the combination of LMWH with compression stockings over stockings alone – none of them in general surgery (1, 38, 42, 47). In all four studies the group employing compression stockings alone is categorized as a placebo group. However, the incidence of VTE in these placebo groups is actually about the same as in previous studies where no prophylactic measures were used. Only one single, rather small study has compared, as we have, the use of LMWH in combination with compression stockings to LMWH alone for VTE prophylaxis. Kalodiki et al. (34), randomized 78 patients undergoing a total hip replacement into three groups:

- a control group without prophylaxis,
- a group which received enoxaparin once daily,
- a group which received enoxaparin and wore graduated compression stockings (TED) for a period of 8-10 days.

All patients had a preoperative perfusion lung scan and a postoperative perfusion-ventilation scan, as well as bilateral ascending phlebography between days 8 and 12. The DVT rates were 93%, 38% and 25%, respectively. No other study comparing LMWH with and without stockings has been published as of today – neither in general surgery nor in any other medical specialty.

The mechanism of action through which compression stockings prevent thromboembolism remains unclear, though it is thought to be multi-functional with a reduction in venous diameter playing the key role. External compression was shown to reduce the overall cross-sectional area of the lower limb and increase the flow velocity within the veins. Compression also appears to improve the evacuation and coaptation of incompetent and incompletely emptied valvular cusps. Reduction in reflux-related stasis and augmented flow velocity could decrease the risk of thrombus formation by reducing venous wall distension, local contact time, and the concentration of coagulation reactants (2, 14, 57, 61, 66).

Despite their widespread use, there is also no agreement as to the most effective stocking design to achieve the above mentioned effects. Thigh-length TED stockings, which are probably employed in most studies, have intended pressures of 18 mmHg at the ankle, 14 mmHg at the calf, 8 mmHg at the knee, 10 mmHg above the knee, and 8 mmHg at the thigh. It is not known whether these pressures are optimal. Moreover, some authors estimate calf-length stockings to be more effective than thigh-length and some prefer non-elastic ones (2, 9, 26). Stocking design is not always specified in the study protocols and, particularly in some of the newer studies, it is not clear whether or not stockings were used at all (18, 27, 30, 44, 59, 41, 36, 52).

Even those stockings believed to be ideally designed may not achieve the warranted effects. A study measuring pressure gradients in patients wearing prophylaxis stockings showed that 98% of the stockings failed to produce the ideal pressure gradient of 18–14–8 from the ankle to the knee; 54% even produced an inverse gradient (7, 62).

Given the recommended pressure gradients intended to be realized by the design of prophylaxis stockings, it remains obscure why other types of compression stockings, e.g., those recommended for the prevention of post-thrombotic syndrome following a deep vein thrombosis, achieve significantly higher pressure ranges (mostly 40-36-21 mmHg) although they must be worn for much longer time periods. These higher pressure compression stockings fail, however, to prevent DVT recurrence, whereas prophylaxis stockings are claimed to reduce DVT incidence by 50% or more (9, 37).

Finally, prophylaxis stockings were conceived for supine patients (61). However, today most patients are mobilized within only a few hours after surgery. Nevertheless guidelines recommend stockings for 5–7 days (61).

Unlike most other studies, ours did not serially screen all our study patients for deep venous thrombosis or pulmonary embolism. The significance of an asymptomatic VTE detected by screening methods such as ^{125}I fibrinogen marking, plethysmography, contrast phlebography, compression sonography, D-dimer testing, or ventilation-perfusion scans is a matter of debate (6, 35, 40, 54). Conclusive evidence that treatment of asymptomatic patients with VTE detected by these methods results in better outcomes is lacking, not only in regard to nonfatal or fatal pulmonary embolism (35), but also in regard to postthrombotic syndrome (25) and pulmonary hypertension (48). Recent study designs have begun to focus more, as we have, on symptomatic thromboembolic events as clinically relevant endpoints (41).

Limitations

We cannot rule out the possibility of diagnostic bias in our study, since the use of stockings cannot be blinded and for organizational reasons we were not able to perform randomization. It is possible that physicians were more likely to order an imaging test for patients who had not received compression stockings than for those who had. Nevertheless, the incidence of symptomatic VTE in our surgical patients was very low with both prophylaxis regimens.

A decline in VTE rates in clinical medicine has been anticipated in recent years (17, 29). Research in this area is lacking, but considering the still doubtless significance of the Virchow triad in regard to VTE pathogenesis, the current prevailing concept of early mobilization is likely to be the most effective measure contributing towards the prevention of thromboembolism in all areas of medicine. New surgical techniques, especially endoscopic and fast track surgery and modern anesthesiologic methods, are

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also reported to reduce VTE rates (49, 51, 53). Furthermore, complicated risk stratification concepts are increasingly being disregarded in favor of simple and effective protocols like the one we used with our surgical patients (24) and finally, new, even more potent, anti-thrombotic agents are being developed (16, 20, 21, 59).

Conclusion

Our data showed that the rate of symptomatic venous thromboembolism in patients on a general surgery ward is kept low when a concept of early remobilization and a simple, but strictly applied protocol of preventative low molecular weight heparin is implemented. Graduated compression stockings did not yield an additional preventive effect with this regimen.

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