CORRESPONDENCE

Clinical Practice Guideline: The Prophylaxis of Venous Thromboembolism

by Prof. Dr. med. Albrecht Encke, Prof. Dr. med. Sylvia Haas, and Prof. Dr. med. Ina Kopp in issue 31–32/2016

Risk Increased During Pregnancy

The risk for developing venous thromboembolism (VTE) is 4–5 times higher during pregnancy. In 80% of cases, this will manifest as deep vein thrombosis of the leg and in 20% as pulmonary embolism (1, 2). VTE is responsible for 20% of deaths associated with pregnancy.

During the postpartum period, the risk of VTE is increased by a factor of 20; one case-control study even showed an increase by a factor of 60 (1). This risk, which persists for two weeks, is highest in the first week postpartum. Since in outpatient births, new mothers leave the hospital on the same day or the day after, increasing numbers of cases of VTE occur outside obstetric wards. For this reason, practices and hospitals jointly carry responsibility for prevention. The risk profile may change during the course of the pregnancy, and this will need to be communicated accordingly. Examples include more severe peripartum or postpartum hemorrhages.

The most important risk factor is prior VTE, with a risk of recurrence of a factor of 25 in persons without thrombophilia. It is not realistic to expect that this might be routinely tested for in a laboratory. But considering the question of Factor V-Leiden mutation is worthwhile, as the homozygotic form is associated with a 35 times higher risk.

These considerations are also relevant in view of a scenario of a rate of cesarean section of 30%; consequently, immobilization in the initial days after the birth will be much more common than after vaginal delivery. Stringent early mobilization and more instruction regarding independent exercises are required, as called for by the authors (3). In spite of a lack of staff in obstetric wards, drug prophylaxis should not gain greater importance than physical prophylaxis.

VTE incidence rates between 0.5 and 1.7 per 1000 births—a difference by a factor of 3 (4)—indicate a clear need for improvement.

DOI: 10.3238/arztebl.2017.0118a

REFERENCES

1. Heit JA, Kobbervig CE, James AH, et al.: Trends in the incidence of venous thromboembolism during pregnancy or postpartum: a 30-year population-based study. *Ann Intern Med* 2005; 143: 697–706.
2. Pomp ER, Lenselink AM, Rosendaal FR, Doggen CJ: Pregnancy, the postpartum period and prothrombotic defects: risk of venous thrombosis in the MEGA study. *J Thromb Haemost* 2008; 6: 632–37.

3. Encke A, Haas S, Kopp I: Clinical practice guideline: The prophylaxis of venous thromboembolism. *Dtsch Arztebl Int* 2016; 113: 532–8.
4. James A: Venous thromboembolism in pregnancy. *Arterioscler Thromb Vasc Biol* 2009; 29: 326–31.

Prof. Dr. med. J. Matthias Wenderlein

Universität Ulm
wenderlein@gmx.de

Conflict of interest statement

The author declares that no conflict of interest exists.

Some Observations on the Prophylactic Recommendation

I wish to thank the authors for their clear introduction to the recent clinical practice guideline “The Prophylaxis of Venous Thromboembolism” (1). I do, however, wish to share some observations with regard to the prophylactic recommendation in living donors of kidneys and livers. In *Table 2* of the article (1), perioperative prophylaxis with heparin is recommended in this setting. The guideline recommendation for thromboprophylaxis in living kidney donors is based on a urological randomized study from 2007 reported by Osman et al. (2), which included a total of 75 patients, allocated to three groups. The groups were randomized to thromboprophylaxis in the form of low molecular weight heparin or unfractionated heparin, or no prophylaxis, respectively. The presented study results, however, relate exclusively to the outcomes of the recipients, not those of the donors. In my opinion, a generalized recommendation for perioperative thromboprophylaxis in living donor nephrectomy can therefore not be made on the basis of this study. In the context of my own literature search, I did not find any other evidence relating to this particular research question either. Regarding thromboprophylaxis in living liver donors, neither the article (1) nor the long version of the clinical practice guideline include relevant references.

Regarding the patient population at our clinic, the risk of developing a venous thromboembolism is assessed by means of a clinical exam and medical history, in accordance with the S3 guideline. In living kidney donors, nephrectomy is undertaken by using minimally invasive retroperitoneoscopic surgery, which usually takes 90–120 minutes. This procedure is therefore in the low-risk category for developing venous thromboembolism (VTE). Donor nephrectomy requires no perioperative medication-based thromboprophylaxis. In our clinic, this is given only after balancing individual patients’ risks, and in the form of low molecular weight heparin. The main emphasis is on early postoperative mobilization of patients, independently of their individual risk of VTE. Since high risk patients are excluded in the context of donor selection, I think

that general medical thromboprophylaxis is not indicated in living kidney donation.

DOI: 10.3238/arztebl.2017.0118b

REFERENCES

1. Encke A, Haas S, Kopp I: Clinical practice guideline: The prophylaxis of venous thromboembolism. Dtsch Arztebl Int 2016; 113: 532–8.
2. Osman Y, Kamal M, Soliman S, et al.: Necessity of routine post-operative heparinization in non-risky live-donor renal transplantation: results of a prospective randomized trial. Urology 2007; 69: 647–5.

Martin Teusch

Klinik und Poliklinik für Hepatobiliäre Chirurgie und Transplantationschirurgie
Universitätsklinikum Hamburg-Eppendorf
m.teusch@uke.de

Conflict of interest statement

The author declares that no conflict of interest exists.

In Reply:

We thank Wenderlein for his comments. His explanations are practice-relevant and reasonable. They might be helpful to readers when implementing the guideline in outpatient practice.

Naturally, we were not able to address all specialist aspects in detail in the article (1). Our article incorporated in the general and special sections covering all 27 disciplines addressed by the guideline and is restricted in terms of coverage and word count. Thus, the article's purpose was to stimulate the use of the long version of the guideline (www.awmf.org/leitlinien/detail/II/003-001.html). Especially obstetrics and gynecology are extensively dealt with in the guideline. All the arguments raised in the letter to the editor are dealt with extensively in the long version.

The epidemiological review by Heit et al. (2) and a review by James et al. (3) were considered and cited in the guideline. The third cited study by Pomp et al. (4) does not add any further data or aspects to the evidence-based conclusions/recommendations of the guideline and therefore does not meet the criteria for inclusion in the reference list as stipulated by the Association of the Scientific Medical Societies in Germany (*Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften*, AWMF).

We wish to thank Teusch too, for his important comment regarding the literature on the prophylaxis of venous thromboembolism (VTE) in the setting of living kidney donation. Indeed, to date only one study has been reported that looked only at thromboprophylaxis in recipients, and which does not support the guideline's recommendation to use prophylaxis in living donors (5). We will clarify this in the accompanying text to the long version of the guideline. However, the recommendation for medical prophylaxis in the setting of living kidney donation with regard to donors derives from the risk assessment for retroperitoneal surgery (nephrectomy) and the special importance of the end-point patient safety in this situation. We therefore do not see any need for changing the recommendation for medical thromboprophylaxis in living donors.

DOI: 10.3238/arztebl.2017.0119

REFERENCES

1. Encke A, Haas S, Kopp I: Clinical practice guideline: The prophylaxis of venous thromboembolism. Dtsch Arztebl Int 2016; 113: 532–8.
2. Heit JA, Kobbervig CE, James AH, et al.: Trends in the incidence of venous thromboembolism during pregnancy or postpartum: a 30-year population-based study. 3 rd. Ann Intern Med. 2005; 143: 697–706.
3. James A: Venous thromboembolism in pregnancy. Arterioscler Thromb Vasc Biol 2009; 29: 326–31.
4. Pomp ER, Lenselink AM, Rosendaal FR, Doggen CJ: Pregnancy, the postpartum period and prothrombotic defects: risk of venous thrombosis in the MEGA study. J Thromb Haemost 2008; 6: 632–37.
5. Osman Y, Kamal M, Soliman S, et al. Necessity of routine postoperative heparinization in non-risky live-donor renal transplantation: results of a prospective randomized trial. Urology 2007; 69 (4): 647 – 51.

Prof. Dr. med. Albrecht Encke

Prof. Dr. med. Sylvia Haas

Prof. Dr. med. Ina Kopp

AWMF-Institut für Medizinisches Wissensmanagement
c/o Philipps-Universität
kopp@awmf.org

Conflict of interest statement

Prof. Haas has received consultancy fees from Bayer, Bristol-Myers Squibb, Daiichi Sankyo, and Sanofi. She has received reimbursement of travel expenses and lecture fees from Aspen, Bayer, Bristol-Myers Squibb, Daiichi Sankyo, and Sanofi.

Prof. Kopp and Prof. Encke declare that no conflict of interest exists.