Obstetric hemorrhage: improving care by collaborating across borders

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Summary

Introduction

Obstetric hemorrhage remains one of the main causes of severe maternal outcome (SMO) in high-income countries. Variations in the incidence of hemorrhage-related SMO between high-income countries exist. The majority of hemorrhage-related maternal deaths and maternal near misses (MNM) can be considered preventable, which implies that the maternal death or MNM could have been prevented by timely and appropriate interventions and access to healthcare of good quality. I hypothesized in this thesis that differences in the incidence of SMO between high-income countries could perhaps be explained by variations in late (second- and third-line) management of obstetric hemorrhage. This hypothesis was assessed in part 1 of this thesis, in which I benchmarked quantitative and qualitative data on severe forms of obstetric hemorrhage between France and the Netherlands, two countries with comparable resources yet variations in hemorrhage-related SMO. Furthermore, to address preventability of hemorrhage-related SMO, in part 2 of this thesis I identified and explored characteristics and management in subgroups of women with SMO due to PPH, as the assessment of subgroups of women suffering SMO has been suggested by the World Health Organization as a tool to further reduce preventable SMO.

Part I. Obstetric hemorrhage: improving maternal outcomes by exploring management strategies in an international context

In **Chapter 2,** I reported considerable variations among guidelines on prevention and management of (severe) postpartum hemorrhage (PPH). Main variations between countries related to (1) prevention of obstetric hemorrhage, such as dose and mode of administration of prophylactic uterotonics; (2) diagnosis of obstetric hemorrhage, such as definition of PPH and methods to measure blood loss; (3) management of hemorrhage with various recommendations as to type and dose of second-line uterotonics and diverging guidance regarding uterine-sparing interventions; (4) recommendations with regard to transfusion thresholds and hemostatic agents; (5) scientific and methodological quality of included guidelines. The results highlight the need for a universal definition of (severe) PPH and for a high-quality standardized, evidence-based guideline and clinical practice algorithm for high-resource settings.

In **Chapter 3**, I presented the results of a systematic review and meta-analysis of the length of the third stage of labor. Currently, there is no consensus on the optimal length of the third stage of labor resulting in varying recommendations in terms of when to proceed to manual removal of placenta. In this chapter, I provided evidence that the risk of adverse maternal outcome increases after 15 minutes of third stage of labor among women with risk factors for PPH. Although these findings emphasize the need to increase vigilance for sings of bleeding among these women, there is currently no robust evidence to recommend earlier manual placenta removal to reduce the risk of adverse outcomes.

In **Chapter 4,** I compared the use of uterine-sparing interventions such as intra uterine tamponade, hemostatic surgery (vascular ligation and compression sutures) and radiological artery embolization to cease bleeding and clinical outcomes between women suffering equally severe PPH in France and the Netherlands. Incidence of SMO was twice as high among women with severe PPH in the Netherlands as compared to France. Obstetricians in France resorted more frequently to second-line uterotonics and uterine-sparing interventions and in an earlier stage of hemorrhage as compared to obstetricians in the Netherlands, which may explain the reported difference in SMO. Nevertheless, I also underlined the high rate of peripartum hysterectomy in France, stressing the need to remain critical about the use of invasive interventions. My findings question the adequacy of uterine-sparing interventions as an indicator for the quality of hemorrhage-related maternity care suggesting the use of other indicators such as those proposed by European Board and College of Obstetrics and Gynaecology (disseminated intravascular coagulation, post-partum hysterectomy, renal failure, cardiac arrest and hemorrhagic shock). Chapter 4 shows that prospective cross-country studies can be a valuable alternative for randomized controlled trials to improve understanding on reported differences in SMO and management strategies.

Chapter 5 contains the results of a binational review of hemorrhage-related maternal deaths in France and the Netherlands. The French and Dutch experts participating in this binational review identified lessons learned. For France, these related mainly to organizational aspects of care and for the Netherlands mainly to clinical aspects of care. This qualitative study highlights the interest of international collaborations on rare events in pregnancy by providing multiple opportunities for care improvement beyond lessons learned in national enquiries. My findings highlight the benefits of including clinicians familiar with different health care systems when performing cross country collaborations. I advocate that cross-country collaborations should be prioritized by governments and

stakeholders in the form of clinical and research exchanges of young obstetricians, and through the facilitation of data sharing.

Part II. Obstetric hemorrhage: reducing preventable severe maternal outcome by exploring subgroups of women with obstetric hemorrhage in France

In **Chapter 6,** I described the evolution of maternal mortality due to obstetric hemorrhage over time in France, which decreased between 2001 and 2015. The proportion of maternal deaths due to PPH by uterine atony dropped significantly while the contribution of surgical injury during caesarean section increased, emphasizing the need to further explore this cause of hemorrhage. Among women who died, we detected fewer instances of substandard transfusion management or critical care after implementation of the national guidelines on PPH in France. Nevertheless, opportunities for care improvement were observed in most recent cases. Our data show that implementing a recurring cycle in which data on maternal deaths due to obstetric hemorrhage are evaluated over time, can provide crucial information on the effectiveness of the implementation of previously formulated recommendations adding to the understanding of improvements that can still be made.

In **chapter 7,** I focused on women who died from hemorrhage due to surgical injury during cesarean section, which emerged as a main contributor to fatal obstetric hemorrhage in France. I describe the profile of women who died from this cause, identifying options for prevention of surgical injury during cesarean section. Main improvable care factors related to a delay in diagnosis and management of hemorrhage. I recommended improving the technical skills around difficult cesarean sections and increasing awareness of those cesarean sections at high-risk of surgical injury. To improve diagnosis, I suggested to include specific guidance on post-cesarean section surveillance by using early obstetric warning scores and the shock index. To reduce delays in management of surgical injuries, I recommended to implement simulation trainings for hemostatic surgery. As this study brought to light that a significant proportion of the women who died gave birth in a low-volume hospital (<1000 births), I suggested to evaluate on a national scale which medical and human resources are necessary to provide acute obstetric care.

Recommendations

In conclusion, potential targets brought to light by my thesis that may improve (the assessment of) hemorrhage-related maternity care, are: (1) a uniform diagnosis and definition for (severe) PPH and improvement of the quality of guidelines on prevention and management of obstetric hemorrhage; (2) adequate indicators to assess quality of hemorrhage-related maternity care; (3) identification of the optimal length of the third stage of labor and the timing of manual removal of the placenta among women with risk factors for PPH; (4) timing and sequence of the use of second-line uterotonics and uterine-sparing interventions in the course of hemorrhage; (5) cross-country collaborations to share data and experiences; (6) prevention, diagnosis and management of surgical injury during cesarean section.