Venous Thromboembolism: A Very Preventable Cause of Maternal Mortality

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With recent media attention on maternal deaths, it is no secret that the maternal mortality rate in the U.S. is an abysmal 26.4 per 100,000 live births as reported in 2015. Countries that we might consider our peers (e.g., United Kingdom, Germany, France, Canada, etc.) all have maternal mortality rates of less than 10 per 100,000 live births. Not only does the U.S. have the highest rate of any high-resource country, but it is the only country in the world outside of Afghanistan and Sudan where the rate is rising.

The leading causes of maternal mortality differ greatly between low- versus high-resource countries, with hemorrhage, sepsis, obstructed labor and hypertension accounting for a larger proportion of deaths in low-resource countries.

A systematic review of maternal deaths by the World Health Organization found venous thromboembolism (VTE) to be the cause in 14.9 percent of maternal deaths in high-resource countries versus approximately 2 percent in low-resource countries. In the U.S., VTE accounted for 9.1 percent of all deaths from 2011-14. The incidence of VTE is increasing over time in women hospitalized for delivery, as risk factors such as obesity, cesarean delivery, advanced maternal age and medical comorbidities increase.
Analyses of maternal deaths in the U.S. have found that pulmonary embolism, with implementation of pharmacologic or mechanical thromboprophylaxis, is one of the most preventable causes of death. The U.K. has seen a dramatic decline in maternal deaths from VTE (18 deaths between 2006-08 compared to 41 deaths between 2003-05) after implementing processes to better identify at-risk women and adopting widespread use of thromboprophylaxis. The California Maternal Quality Care Collaborative (CMQCC) recognized that 40 percent of California maternal deaths were preventable, and the state has seen a 55 percent decline in maternal mortality since 2006 after developing state-wide outreach collaboratives and quality-improvement toolkits, one of which focuses on VTE.

Armed with this knowledge, the physician anesthesiologist has a unique opportunity to improve outcomes in maternal health care, and the road map to do so is available for free of charge. The Council on Patient Safety in Women's Health Care includes ASA, the American Association of Nurse Anesthetists, American College of Obstetricians and Gynecologists (ACOG), Society for Obstetric Anesthesia and Perinatology (SOAP) and many other professional organizations with the vision of providing “safe health care for every woman.” The website safehealthcareforeverywoman.org has accessible patient safety bundles published by the National Partnership for Maternal Safety (NPMS) under the guidance of the Council on Patient Safety in Women's Health Care. In addition, the website has tools aimed at reducing maternal morbidity and mortality. The bundles outline critical clinical practices that should be implemented on every maternity unit. The CMQCC also has a free toolkit, “Improving Health Care Response to Maternal Venous Thromboembolism,” available since March 2018 and consistent with the toolkit provided by the NPMS.

The VTE patient safety bundle from the NPMS is divided into four sections:

1. Readiness – Use standardized VTE risk-assessment tools in every unit during outpatient prenatal care, antepartum hospitalization, hospitalization for birth and the postpartum period.
2. Recognition and Prevention – Use risk-assessment tools on all patients to identify those appropriate for thromboprophylaxis in addition to providing education to patients and health care providers.
3. Response – Use standardized recommendations in every unit for mechanical prophylaxis and dosing and timing of pharmacologic prophylaxis.

The NPMS Consensus Bundle on VTE addresses the differing recommendations for prophylaxis among the Royal College of Obstetricians and Gynaecologists (RCOG), ACOG and the American College of Chest Physicians. Commonly in the U.S., only women with the highest risk of VTE receive prophylaxis, which is in contrast to the U.K., where risk factor assessment is routinely performed for all parturients and a much greater percentage of women receive thromboprophylaxis. The resulting recommendations in the NPMS bundle advise administering prophylaxis to more women than is the current practice in the U.S., but fewer than indicated by the RCOG recommendations. The U.K. has an excellent track record of reducing maternal VTE, and the RCOG recommendations may prove superior in the future.

The goal of the NPMS is adoption of its safety bundles by every birthing facility in the U.S. As leaders in patient safety, physician anesthesiologists should participate in multidisciplinary teams to implement the bundles and reduce maternal mortality in our country.

More frequent use of pharmacologic thromboprophylaxis for hospitalized parturients raises concern among anesthesiologists about the safety of neuraxial anesthesia. SOAP responded to this concern with the 2018 publication of a consensus statement addressing parturients receiving anticoagulants. This statement recognizes the elevated risk of VTE in pregnant and postpartum women in contrast to the very low incidence of spinal-epidural hematomas in pregnant women, including those receiving thromboprophylaxis. It summarizes studies on the altered pharmacokinetics of unfractionated heparin (UFH) and low-molecular weight heparin (LMWH) in the pregnant population and provides guidance for the use of neuraxial anesthesia in ante-, intra- and postpartum patients receiving UFH and LMWH (Table 1, page 11). Included in the statement are decision aids for use in urgent and emergent situations. The 2018 American Society of Regional Anesthesia and Pain Medicine (ASRA) update and the app address the situation of the anticoagulated parturient for neuraxial block, suggesting that the guidelines be applied to parturients. Both the SOAP and ASRA statements agree that

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consideration be given to performing neuraxial blockade in select situations where general anesthesia presents a greater risk than spinal epidural hematoma to the parturient. SOAP supports the use of both NSAIDs and low-dose thromboprophylaxis after epidural catheter removal for patients following cesarean delivery given the extensive clinical practice of using these medications together and benefit of reducing opioid use. Prior to catheter removal, it recommends avoiding NSAIDs if UFH or LMWH are being administered.13

The goal of the NPMS is adoption of its safety bundles by every birthing facility in the U.S.12 As leaders in patient safety, physician anesthesiologists should participate in multidisciplinary teams to implement the bundles and reduce maternal mortality in our country. These strong and evidence-based practice recommendations will likely result in the increased use of pharmacologic thromboprophylaxis in pregnant and postpartum patients but should not deter the continued use of safe neuraxial anesthesia. Multidisciplinary communication about anticoagulation status is crucial, and institutions should develop effective methods to communicate among services when patients receiving thromboprophylaxis may need delivery. By following the consensus statements of the NPMS and SOAP, we can bring about these safe and necessary changes to clinical practice.

References:
**Table 1: Timing of Neuraxial Block After Anticoagulation**

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>Antepartum/Intrapartum</th>
<th>Postpartum</th>
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</thead>
<tbody>
<tr>
<td>Low dose SQ UFH (5,000 U bid or tid)</td>
<td>Wait 4-6 hours after last dose or check aPTT (proceed if within normal range)</td>
<td>Wait 1 hour after neuraxial block placement and 1 hour after removal of epidural catheter to initiate or resume thromboprophylaxis. Indwelling catheters can be maintained with 5,000 U SQ bid UFH. Removal of catheter can occur 4-6 hours after last dose, and redosing can occur 1 hour after removal of the epidural catheter.</td>
</tr>
<tr>
<td>Intermediate dose SQ UFH (7,500-10,000 U bid with total &lt;20,000 U/day)</td>
<td>Wait 12 hours after last dose or check aPTT (proceed if within normal range)</td>
<td>Same as for low dose SQ UFH postpartum recommendations.</td>
</tr>
<tr>
<td>High dose SQ UFH (&gt;10,000 U/dose or total &gt;20,000 U/day)</td>
<td>Wait 24 hours after last dose and check aPTT (proceed if within normal range)</td>
<td>Same as for low dose SQ UFH postpartum recommendations.</td>
</tr>
<tr>
<td>Low dose SQ LMWH (enoxaparin 30 mg BID or ≤ 40 mg qd)</td>
<td>Wait 12 hours after last dose</td>
<td>Wait 12 hours after neuraxial block and 4 hours after removal of epidural catheter to initiate or resume thromboprophylaxis. Indwelling catheters can be maintained with low dose SQ LMWH. Removal of catheter can occur 12 hours after last dose, and redosing can occur 4 hours after removal of the epidural catheter.</td>
</tr>
<tr>
<td>Intermediate dose LMWH (enoxaparin &gt;40 mg qd or 30 mg bid and &lt;1 mg/kg bid or 1.5 mg/kg qd)</td>
<td>No published data to recommend a specific interval between 12-24 hours after last dose</td>
<td>No data</td>
</tr>
<tr>
<td>High dose SQ LMWH (enoxaparin 1 mg/kg bid or 1.5 mg/kg qd)</td>
<td>Wait 24 hours after last dose</td>
<td>Wait 24 hours after neuraxial block and 4 hours after removal of epidural catheter to initiate or resume thromboprophylaxis. Avoid therapeutic dosing with in situ epidural catheters.</td>
</tr>
<tr>
<td>I.V. heparin</td>
<td>Wait 4-6 hours after last dose and check aPTT (proceed if within normal range)</td>
<td>Same as for low dose SQ UFH postpartum recommendations.</td>
</tr>
</tbody>
</table>

UFH: unfractionated heparin
LMWH: low molecular weight heparin

The risk of spinal epidural hematoma associated with placement of the neuraxial block should be balanced against the risks of general anesthesia, taking into consideration co-existing conditions and urgency of the clinical scenario.

Use of NSAIDS along with anticoagulants while an epidural catheter is in place can increase the risk of bleeding complications.