An Early Anti-Inflammatory Response Is Followed by Pro-Inflammatory Response in Hip Fracture Patients

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Purpose: Early inflammatory response to trauma may be involved in venous thromboembolism (VTE). Vessel wall inflammation triggers pro-inflammatory cytokine formation (including interleukin (IL)-6 and tumor necrosis factor-alpha (TNF-α), which activates the coagulation system through tissue factor (TF) induction. In contrast, IL-10, an anti-inflammatory cytokine, inhibits TF expression. Given high VTE risk after hip fracture surgery (HFS), we performed serial inflammatory marker analysis to quantify the inflammatory response following HFS.

Methods: Consecutive HFS patients >50 years of age were recruited. Blood was collected and processed for serum every 24-hours from admission until postoperative day (POD) 5, then in follow-up at 2 and 6 weeks. Serum analyses of cytokine levels were performed using a Milliplex human pro-inflammatory panel of 13 cytokines. Cytokine levels at each time were compared to admission levels using paired t tests.

Results: 52 patients (34 female, mean age 78.5 years, SD [standard deviation] 11.0) were included. Mean IL-10 levels were highest on admission (29.8, SD 81.5), and declined below admission levels by POD 3 (6.5, SD 5.3, $P = 0.05$). In contrast, mean IL-6 levels were significantly elevated on POD 1 (37.9, SD 56.7) compared to admission (17.5, SD 13.6, $P = 0.01$) and declined below admission values by POD 5 (7.6, SD 6.3, $P < 0.001$). TNF-α levels were higher on POD 3 (24.4, SD 17.5) compared to admission (20.3, SD 16.0, $P = 0.05$) and remained elevated at 2 weeks (26.7, SD 31.5, $P = 0.1$). Admission IL-6 and IL-10 were significantly elevated compared with POD 5, 2-week, and 6-week follow-up, indicating an early inflammatory response to injury that can be measured at the time of admission (Fig. 1).

Conclusion: There is a systemic inflammatory response following hip fracture. IL-10 may play an important role in decreasing the pro-inflammatory response following hip fracture and surgery. Further understanding of the inflammatory response following HFS may lead to novel target development for VTE prevention in this high-risk population.

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