smoking volunteers. Patients 19 to 60 years of age who smoked at least 1 pack per day were given 1.5 to 3.0 mg warfarin daily for 14 days. After a 1-month washout of not smoking, patients took the same warfarin dose for 14 days. Three patients dropped out because they returned to smoking. Steady-state warfarin levels measured on days 11 to 14 of each phase were averaged for each subject.

The steady-state warfarin level in the nonsmoking phase was 0.45 mg/L compared with 0.40 mg/L in the smoking phase ($P<.01$). Prothrombin times were not measurably different between groups. A 2011 systematic review (N=3,386) examined 12 cross-sectional studies (7 prospective, 5 retrospective) and the crossover study above investigating the interactions between tobacco use and warfarin therapies. Three studies (n=1,783) that reported the outcome as percent difference in warfarin dosing showed smokers required 12% higher warfarin doses (95% CI, 7.0–17) than nonsmokers. The mean age in these 3 studies ranged from 58 to 65 years. There was no heterogeneity among these studies. Three other studies (n=544), with significant heterogeneity, reported the outcome as absolute difference in warfarin dosage. They showed smokers required a nonstatistically significant 2.3 mg per week higher dose of warfarin compared with nonsmokers (95% CI, –2.5 to 7.0). The mean age in these 3 studies ranged from 59 to 69 years.

A 2001 case report describes an 80-year-old man who had been taking 5 mg warfarin daily for stroke and had INR values in the 2.0 to 3.0 range for 10 months. He had a 50 pack-year history of smoking. INR values steadily increased the 3 months after smoking cessation to a peak of 3.7. His warfarin dose was reduced from 35 to 30 mg weekly. INR was stable on the new dose for 9 months. No changes in prescription medications, over-the-counter medications, herbal medications, or alcohol were reported.

A 2005 case report describes a 58-year-old man with a history of deep vein thrombosis who was admitted with bacterial meningitis. Prior to admission he took 58.75 mg per week of warfarin and had stable INR values for 6 months. He received multiple antibiotics during the admission. On discharge, he resumed his usual 3 to 5 glasses of wine each day, but not tobacco (39 pack-years). Two months after the antibiotics were discontinued, elevated INRs of 3.4 then 5.5 were reported on his previous warfarin dose. His dose was ultimately reduced to 43.75 mg per week, which resulted in stabilized INRs at or near the target range.

Nancy Robertson, PharmD  
Matthew Ludemann, MD  
Kenneth Soda, MD  
St. Anthony North FMRP  
Westminster, CO


Does manual extraction of the placenta or manual exploration of the uterus increase the risk of endometritis?

Evidence-Based Answer

Manual extraction of the placenta appears to increase the risk of endometritis after vaginal or cesarean delivery (SOR: B, cohort study and RCT). In 1995, a retrospective cohort study of more than 25,000 deliveries compared manual removal of the placenta with spontaneous delivery of the placenta after vaginal delivery. A total of 1,421 deliveries had manual removal of the placenta and 24,266 deliveries involved spontaneous delivery of the placenta of which, 1,227 and 1,278, respectively, were randomly selected. After exclusion criteria (postpartum antibiotics and neonates weighing <550 g or <20 weeks’ gestation), records were available for 1,052 deliveries with manual extraction of the placenta and 1,085 with spontaneous delivery of the placenta. Endometritis was defined as temperature >38°C and physician impression, or any patients treated for endometritis postpartum regardless of temperature.

Manual removal of the placenta was associated with an increased risk of endometritis (OR 2.9; 95% CI, 1.7–4.9; NNH=20). In 2005, a prospective RCT of 840 cesarean deliveries evaluated the incidence of endometritis after manual extraction of the placenta compared with spontaneous delivery of the placenta. All women with an indication for cesarean section were randomized into 2 subgroups: manual placental delivery (n=420) and spontaneous placental delivery (n=420). Exclusion criteria included intrapartum antibiotics, chorioamnionitis, emergency cesarean hysterectomy, rupture of membranes for...
>12 hours, bleeding diathesis, abnormal placentation, and prior postpartum hemorrhage. All patients received 1 g cefazolin after clamping of the umbilical cord. Endometritis was defined as temperature of ≥38°C on 2 occasions 6 hours apart after the first postoperative day and 2 of the following signs or symptoms: foul-smelling lochia, leukocytosis (white blood cell count >15,000/mL), or uterine tenderness.

The incidence of postoperative endometritis was significantly higher with manual removal of the placenta than with spontaneous delivery of the placenta (15% vs 5.7%; OR 3.0; 95% CI, 1.8–4.9; NNH=10).²

Evidence-Based Answer

The answer is unclear. In nulliparous women with singleton pregnancies presenting in spontaneous active labor, there is conflicting evidence that IV fluids at more than the standard rate of 125 mL/h shorten labor (no SOR given).

A 2012 RCT evaluated the rate of IV fluid administration on the duration of labor in 293 nulliparous women.¹ Low-risk nulliparous women in active labor received oral hydration alone, lactated Ringer’s at 125 mL/h, or lactated Ringer’s at 250 mL/h.

The duration of labor among the 3 groups was not significantly different: 391 minutes in the oral fluid group, 363 minutes in the 125 mL/h group, and 343 minutes in the 250 mL/h group (P=.20 for 3-way comparison). Labor lasting longer than 12 hours occurred in 7.1%, 4.1%, and 3.1%, respectively (P=.42 for 3-way comparison). Need for oxytocin administration was 37%, 32%, and 33%, respectively (P=.68 for 3-way comparison).³

A 2006 RCT evaluated the effect of IV fluid rates on labor length in 300 low-risk nulliparous women with singleton pregnancies over 37 weeks’ gestation in spontaneous active labor.² Mean length of labor was decreased in the 250 mL/h group compared with the 125 mL/h group (253 vs 386 minutes; P=.0001). Labor lasting longer than 10 and 15 hours was less common in the 250 mL/h group (13.8% vs 8.1%; P=.001; 4.5% vs 0%; P=.02). Need for oxytocin administration was significantly less in the high rate group (20.4% vs 8.1%; P=.001).

A 2000 RCT evaluated the effects of IV fluid rates on the length of labor in 195 nulliparous women.³ Patients at more than 36 weeks’ gestation in active labor received lactated Ringer’s or isotonic sodium chloride solution at a rate of 125 or 250 mL/h. Labor lasting longer than 12 hours occurred more frequently in the 125-mL group (26% vs 13%; P=.047). Need for oxytocin administration was no different between the 125-mL group and the 250-mL group (65% vs 49%; P=.06). Rate of cesarean deliveries between the 2 groups was no different (17% vs 10%; P=.22).

Evidence-Based Answer

Wearing high heels (HH) habitually leads to multiple changes in a person’s biometrics, including increased lower extremity tendon stiffness, increased lumbar lordosis, and a more retroflexed pelvis, but inconsistent changes in muscle fascicle shortening (SOR: C, disease-oriented evidence from small cohort trials). Whether these changes cause symptoms is not known.

A cohort study done in 2012 examined muscle fascicle length and strain markers in the lower extremity of habitual HH users versus nonusers during barefoot standing and walking.¹ The sample group included 9 women who had worn heels 5 cm high for at least 40 hours a week for at least the past 2 years. The control group consisted of 10 women who did not regularly wear heels. The study does not state how participants were recruited. Measurements were taken using a mixture of surface electromyography and ultrasound.