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1 **Pulse wave analysis by digital photoplethysmography to record maternal hemodynamic**
2 **effects of spinal anesthesia, delivery of the baby, and intravenous oxytocin during**
3 **cesarean section**

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25 **Abstract**

26 **Objective:** To investigate changes in maternal ECG ST index, blood pressure (BP), cardiac
27 left ventricular (LV) ejection function and vascular tone/stiffness in large and small arteries
28 occurring during elective cesarean section (CS) in spinal anesthesia.

29 **Material and methods:** 26 women were monitored with photoplethysmographic digital pulse
30 wave analysis (DPA) before and after spinal anesthesia, after delivery of the baby, after 5 IU
31 oxytocin bolus IV, and 5 minutes later. Statistics with Wilcoxon matched-pairs signed-rank
32 and Friedman tests at a $p < 0.05$ were performed.

33 **Results:** Spinal anesthesia resulted in significantly decreased BP, increased ST index and LV
34 ejection time, and small-artery vasodilation. Delivery of the baby resulted in global
35 vasoconstriction and increases in systolic BP and heart rate (HR). Oxytocin lowered BP, HR
36 and ST index, increased LV ejection power and caused both large- and small-artery
37 vasodilation. ST index and BP recovered after 5 minutes, but low HR and low vascular tone
38 persisted.

39 **Conclusions:** Spinal anesthesia and oxytocin caused arterial vasodilation and cardiac
40 affection. Oxytocin caused a decrease in HR despite a fall in BP, indicating a direct negative
41 chronotropic effect. Delivery of the baby caused momentous cardiovascular changes, possibly
42 due to maternal emotions and auto-transfusion of blood from the uterus.

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44 **Key words:** arterial elasticity; arterial stiffness; oxytocin; pregnancy; pulse wave analysis;
45 spinal anesthesia.

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49 **Introduction**

50 Oxytocin is routinely administered at cesarean section (CS) to contract the uterus and prevent
51 hemorrhage. However, many women then experience discomfort, nausea, and chest pain.

52 These symptoms have been attributed to the significant circulatory dose-dependent effects of
53 oxytocin [1] including ECG ST-depression, increase in heart rate (HR), stroke volume and
54 cardiac output (CO), and decrease in systemic vascular resistance and arterial blood pressure
55 (BP).[2-8] Detailed studies of the immediate hemodynamic response show an increase in HR
56 and decreases in systemic vascular resistance and BP within 30-40 seconds after a 5 U
57 oxytocin bolus, with a concomitant increase of CO, followed by a rebound decrease in HR
58 and a slow restitution of the BP.[5,9]

59 Pharmacological vascular effects can be studied by analyzing pulse wave (PW) curve contour
60 characteristics, determined by propagation of the forward percussion PW along the vascular
61 tree and the reflection of the tidal PW from distal arteries. PW characteristics can be
62 determined by digital PW analysis (DPA), which is a rapid, non-invasive and operator-
63 independent photoplethysmographic (PPG) method. The DPA has been validated against
64 invasive aortic measurement and correlates well with radial pulse applanation tonometry.
65 [10,11] The DPA method can assess cardiac ejection time and distinguish between vascular
66 tone/stiffness in large and small arteries.[11]

67 The primary objective of the study was to investigate the effects of oxytocin during elective
68 CS on cardiac left ventricular (LV) ejection function and systemic arterial stiffness. We
69 hypothesised that oxytocin decreases arterial vascular tone, but there is no knowledge yet
70 whether oxytocin affects both large and small arteries.

71 Spinal anesthesia is frequently associated with maternal hypotension despite precautions with

72 plasma volume expansion and vasopressor substances.[12] The secondary objectives of the
73 study were to investigate the cardiovascular effects of spinal anesthesia and delivery of the
74 baby; due to adjunctive effects of fluid co-load and vasopressors, and to a lack of previous
75 studies with the DPA method, we could not settle any hypotheses for these aims.

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95 **Material and Methods**

96 *Study design*

97 The study was prospective, with no interventions added to the routine management, carried
98 out at the Skåne University Hospital in Lund, Sweden. Women who met the inclusion criteria
99 were recruited consecutively and gave their informed consent to be monitored by a Meridian
100 DPA during elective CS in spinal anesthesia. The study recordings were all performed by one
101 of the authors (S.R.). The study was approved by the Regional Research Ethics Committee in
102 Lund (Dnr 2012/649).

103 The inclusion criteria were healthy women at ≥ 34 gestational weeks scheduled for elective
104 CS in spinal anesthesia with singleton pregnancy and informed consent. The exclusion criteria
105 were hypertension, preeclampsia, abnormal pregnancy with expected surgical problems,
106 coagulopathy, cardiovascular disease, American Society of Anesthesiologists physical status
107 classification system (ASA-class) III or more, disease of upper extremities impeding
108 measurements, or women unwilling to participate.

109 The pre-defined drop-out factors were blood loss greater than 1000 mL within the time frame
110 of DPA measurements, initial dose of oxytocin other than 5 IU (8.35 μg), insufficient
111 anesthesia, conversion to general anesthesia, administration of other vasoactive or uterotonic
112 drugs than in the protocol, other deviations from the study protocol, technical errors, or
113 patient unwilling to participate further.

114 *Study protocol*

115 All recordings were performed during maternal quiescence in the supine position, with the
116 operation table tilted approximately 15 degrees to the left. 2 L/min of oxygen was delivered
117 through the nasal route throughout the procedure. All women were connected to a Philips

118 Intellivue MP70 (Philips Healthcare, Stockholm, Sweden) surveillance device and
119 continuously monitored with an oxygen saturation probe, an automatic BP cuff and a 3-lead
120 ECG. From this was derived the ST index, a summation of the absolute values from ECG
121 leads V2, V5, and aVF.[13] For the DPA measurements, the PPG probe (Meridian DPA,
122 Meridian Co., Ltd. Korea, and Salcor AB, Uppsala, Sweden), connected to a laptop (HP 625,
123 Hewlett Packard, Solna, Sweden), was placed on the right second or third finger.

124 The baseline measurement (T0) was made after 5 minutes of rest before spinal anesthesia. The
125 next recording (T1) was made 15 minutes after spinal anesthesia, i.e. just before the start of
126 surgery. Measurement T2 was made immediately after delivery of the baby, but before
127 oxytocin administration and further surgery. Immediately after the T2 recording was finished
128 and the umbilical cord was clamped, a 5 IU (8.35 µg) bolus of oxytocin (Syntocinon, Swedish
129 Orphan AB, Stockholm, Sweden) was given IV during 60 seconds. When the bolus was
130 finished, a stopwatch was started and 60 seconds later the next DPA recording was started
131 (T3). The DPA recordings were then continued with measurements 5 minutes after the bolus
132 was finished (T4).

133 The BP was measured intermittently every 2 minutes as well as immediately after at each T
134 recording point. The measurements were performed in the contralateral arm to avoid
135 interference with the DPA measurements. Recordings of ST index, HR, and systolic and
136 diastolic BPs (SBP, DBP) were noted manually in a case report form at each T point. The
137 volumes of blood loss and IV fluid given, vasopressor treatment, as well as any other specific
138 treatment were also noted in the case report form at each specific T point.

139 Spinal anesthesia was administered with the patient sitting. The standard dose was
140 bupivacaine hyperbaric solution 5 mg/mL (Marcain Tung, AstraZeneca, Södertälje, Sweden)

141 2 mL (10 mg) mixed with 1 mL sufentanil 5 μ g/mL (Sufenta, Janssen-Cilag, Sollentuna,
142 Sweden). Short women (< 160 cm) received 9 mg of bupivacaine (n=3) and tall women (>179
143 cm) received 12 mg (n=1). After approximately 15 minutes preoperative preparation time,
144 spinal anesthesia depth and spread was tested with pinprick and cold, and then surgery was
145 allowed to start.

146 The protocol for plasma volume expansion implicated co-loading with RingerAcetat
147 (Fresenius Kabi, Uppsala, Sweden), approximately 20 mL/kg in the first 20 min, starting after
148 the baseline measurement (T0), followed by 5-10 mL/kg during the rest of the procedure. In
149 case the blood loss was > 500 mL, or if clinical signs of hypovolemia occurred (low BP,
150 tachycardia, poor capillary perfusion), 500 mL of Venofundin (B. Braun Medical, Danderyd,
151 Sweden) could be given. Greater blood loss than 1000 mL was an exclusion criterion.

152 The protocol for vasoactive drugs implicated the use of phenylephrine 50-100 μ g IV if mean
153 arterial pressure (MAP) fell below 20% of baseline, or below 60 mmHg, or if clinical signs of
154 low BP occurred, such as nausea or pallor. Atropine or ephedrine was administered in case of
155 bradycardia. This standard protocol was used also after the delivery of the baby.

156 *Digital photoplethysmography*

157 The physiological background to the DPA method has been described previously.[10,14] The
158 Meridian DPATM reports 17 different parameters, but for this study we selected parameters
159 with the best repeatability and best correlation to gold standard applanation tonometry: pulse
160 height (PH), aging index (AI), ejection time compensated (ETc), cardiac ejection elasticity
161 index (EEI), dicrotic index (DI), dicrotic dilation index (DDI), and the ratios *b/a* and *d/a*. [11]
162 Descriptions of the parameters are shown in Table 1.

163 The DPA method cannot distinguish between decreased arterial wall elasticity due to
164 structural remodeling of the arterial wall (aging, vascular disease), low compliance
165 due to vascular volume expansion, or vasoconstriction; in the literature and in this
166 paper, the terms “vascular tone” and “stiffness” are used interchangeably.

167 *Statistical analyses*

168 Some of the DPA variables are HR dependent [11] and the statistical analyses were
169 accordingly performed with both crude and HR-adjusted DPA values. If simple linear
170 regression analyses between HR and a DPA variable at T0 yielded a statistically significant
171 correlation ($p < 0.05$), and the intervention (spinal anesthesia, delivery of baby, oxytocin
172 administration) resulted in a significant change in HR, the DPA variable in question was
173 adjusted to a HR of 75 bpm, denoted DPA@75, with the equation $DPA@75 = DPA + C(75 -$
174 $HR)$. C denotes the slope constant.

175 The cardiovascular effects of spinal anesthesia were analyzed with recordings from point T0
176 to T1, the effects of the start of surgery and the delivery of the baby between T1 to T2, and
177 the effects of oxytocin were analyzed with recordings T2-T3-T4. The longitudinal changes in
178 single T-T steps were analyzed with the Wilcoxon matched-pairs signed-rank test with a two-
179 sided p value < 0.05 considered significant. To evaluate the risk of type I errors the Friedman
180 non-parametric one-way ANOVA for repeated measurements T2-T3-T4, and Holm-
181 Bonferroni adjustments of the p values achieved at the Wilcoxon tests, were also calculated:
182 in the three T2-T3, T3-T4 and T2-T4 comparisons the Holm-Bonferroni significance level is
183 $< 0.05/3$ equal to < 0.0167 for the Wilcoxon test with the lowest p value, $< 0.05/2$ equal to $<$
184 0.025 for the second lowest, and $< 0.05/1$ equal to < 0.05 for the third.

185

186 **Results**

187 Among the 26 recruited women, three women were excluded from DPA analyses from T3 and
188 onwards because they were given a bolus of 10 IU (16.70 μg) oxytocin instead of 5 IU. In five
189 women the measurements T0-T1 (spinal anesthesia) could not be analyzed due to technical
190 recording errors at T0, but they were included in the measurements T1-T4. Six women had
191 missing ETc, EEI, or DDI values at T2 and/or T3.

192 At T0 significant correlations were only found between HR and EEI ($p = 0.037$, $R^2 = 0.22$)
193 and DDI ($p = 0.048$, $R^2 = 0.20$).

194 *Effects of spinal anesthesia (T0-T1)*

195 From measurement point T0 to point T1 the HR was not affected and hence no HR-
196 adjustments of DPA parameters were made. Spinal anesthesia resulted in significant decreases
197 in SBP and DBP and an increase in ECG ST index (Table 2, Figure 1). The DPA parameters
198 PH, DI, and DDI showed peripheral/small-artery vasodilation; ETc indicated increased LV
199 ejection time suggesting decreased CO and/or large-artery vasoconstriction, while EEI (large-
200 artery stiffness, LV ejection capacity), b/a (large-artery stiffness, LV ejection capacity), d/a
201 (small-artery stiffness) and AI (global vascular stiffness) were unchanged.

202 *Effects of surgery and delivery of the baby (T1-T2)*

203 The HR increased significantly from T1 to T2 and the DPA parameters EEI and DDI were
204 accordingly adjusted to EEI@75 and DDI@75, respectively. After the start of surgery and
205 delivery of the baby (point T2), the SBP increased significantly but the DBP and MAP as well
206 as the ST index remained unchanged (Table 2, Figure 1). A large-artery vasoconstriction
207 and/or decreased LV ejection power were indicated by significant changes of b/a and
208 EEI@75, a marginally significant small-artery vasoconstriction by DI ($p = 0.062$), and a

209 global arterial vasoconstriction by AI. No significant changes were found for PH, ETc, and
210 *d/a*.

211 ***Effects of oxytocin (T2-T4)***

212 The hemodynamic effects of oxytocin are shown in Table 3 and Figure 1. The HR decreased
213 significantly at T2-T3, and EEI and DDI were accordingly HR-adjusted.

214 From T2 to T3 the oxytocin injection resulted in significant decreases in DBP and MAP as
215 well as in ST index, but the SBP remained unchanged (Table 3, Figure 1). A large-artery
216 vasodilation and/or increased LV ejection power were indicated by a significant change of
217 EEI@75, and a small-artery vasodilation by PH. No significant changes were found for ETc,
218 DI, DDI@75, *b/a*, *d/a* and AI.

219 Restitution to T2 values of the DBP, MAP and ST index had occurred at point T4, 5 minutes
220 after the oxytocin bolus. The initial T2-T3 changes in HR and PH were still significant at T4.
221 In addition, from T3 to T4 changes in *d/a* and AI indicated small-artery and global
222 vasodilation. Throughout T2-T3-T4, oxytocin had no significant effects on SBP, ETc, DI,
223 DDI@75 and *b/a*.

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231 Discussion

232 The procedures with spinal anesthesia, intravenous fluids, vasoactive drugs and delivery of
233 the baby and placenta make it problematic to interpret the hemodynamic effects of oxytocin at
234 CS. In addition, relief of aorto-caval compression when emptying the uterus, bleeding and
235 maternal emotions may interfere.[15] At the start of the serial post-oxytocin recordings,
236 significant circulatory changes had already occurred. Spinal anesthesia, and the concomitant
237 procedures, resulted in a vasodilation of small arteries and peripheral hyperemia,
238 accompanied by a fall in both SBP and DBP and an increase in the ECG ST index. Even so,
239 the DPA parameter ETc increased, indicating a prolongation of the LV ejection time,[11] i.e.
240 large-artery vasoconstriction and/or a decrease in CO. The ETc elevation could be an effect of
241 phenylephrine, a vasoconstricting alpha-1-adrenergic receptor agonist with well-known side
242 effects of decreased HR and CO.[16]

243 Start of surgery and delivery of the baby resulted in increases of HR and SBP and a global
244 vasoconstriction. A further deepening of the spinal anesthesia during this time interval is not
245 unlikely, but would have a further vasodilatory effect. We found no previous studies
246 addressing the hemodynamic effects of the cesarean delivery procedure *per se*, but it seems
247 clear that surgery and delivery of the baby had profound effects on the maternal circulation.
248 During surgery and delivery of the baby the mother is exposed to both positive and negative
249 mental stress and, in addition, the circulatory effects could be due to a catecholamine surge or
250 auto-transfusion of blood from the empty and shrunk uterus.

251

252 Negative stress triggers increases in oxygen consumption, respiration, BP, CO, and peripheral
253 vascular resistance, whereas relaxation responses are mostly the opposite. [17] Sinha et al.
254 [18] found that in healthy young males happiness induces increases in HR and SBP, decreases

255 in LV ejection time, stroke volume and peripheral vascular resistance, whereas DBP and CO
256 remain unaffected. In accordance, watching a comedy induces a rise in BP and vasodilation.
257 [19]

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259 Regarding auto-transfusion of blood, the effects of acute blood volume expansion have been
260 investigated in experiments on healthy animals and humans. Jandhyala & Hom [20] showed
261 in dogs that blood transfusion significantly increased BP and central venous pressure and
262 reduced HR. The decrease in HR was explained by a reflex compensation to the elevated BP.
263 Increases in systemic BP and central venous pressure have been shown in several animal and
264 human studies, with linear relations between the magnitudes of volume expansion and
265 increase in pressure. [21-23] Most of the transfused blood is pooled in the low pressure
266 vasculature, acting as a distensible reservoir. [21-23]

267

268 To study the isolated effect of blood volume expansion on vascular smooth muscles,
269 Jandhyala & Hom [20] denervated the vasculature in a hind limb of dogs. By volume
270 expansion the vascular resistance increased. However, in other vascular beds a volume
271 expansion may result in a decrease in vascular resistance, as demonstrated in the pulmonary
272 vasculature in dogs. [22] Thus, the findings in our study could point to a combined
273 hemodynamic effect of maternal emotions and blood volume expansion: the increase in HR
274 being a result of positive emotions, the increase in SBP being a result of positive emotions
275 and auto-transfusion of blood, and the increase in vascular tone being a result of auto-
276 transfusion.

277 A 5 IU IV oxytocin bolus given during 60 seconds resulted within 1-5 minutes in a
278 vasodilation of both large and small arteries, accompanied by a fall in HR, DBP and ST index.

279 Since the normal response to a decline in BP due to vasodilation would be an increase in HR,
280 the findings indicate a direct negative chronotropic effect of oxytocin. Although none of the
281 women in the present series experienced chest pain or discomfort, the findings point to a
282 transient cardiac ischemia caused by oxytocin. The coronary arteries are perfused mainly
283 during diastole, but since oxytocin tended to slow down the HR rather than to increase it, and
284 the LV ejection time was not significantly affected, a shortening of diastole was not
285 etiological of ischemia. An alternative mechanism to cardiac ischemia caused by oxytocin is
286 coronary vasoconstriction, which has been demonstrated in dogs.[24]

287 Five minutes after the oxytocin administration, a global vasodilation and fall in HR persisted,
288 but the DBP and ST index had returned to levels recorded before the oxytocin administration.
289 Hence, the vasodilation and negative chronotropic effects were not just transient.

290 Previous studies on IV oxytocin bolus effects during CS have shown a decrease in peripheral
291 vascular resistance and a positive chronotropic effect resulting in an increase in CO.[5,7] In
292 contrast, we found a negative chronotropic effect lasting for at least 6 minutes and a possible
293 positive inotropic effect as indicated by a rapid increase in EEI (increased LV ejection
294 power). Also animal studies have shown a negative chronotropic effect, [2,25] but the
295 inotropic effect is not clear, since studies have shown a decrease in LV contraction force [2]
296 as well as an increase.[25] Cardiac synthesis of oxytocin and oxytocin receptors have been
297 found in rats and dogs, [2,26] suggesting not only a systemic vascular effect of oxytocin but
298 also direct cardiac effects by autocrine and/or paracrine pathways.

299 The divergent results can possibly be explained by the fact that oxytocin has a biphasic
300 vascular effect, as demonstrated by Thomas et al. [5] and Moertl et al. [9]: within the first
301 post-oxytocin minute the HR increases and the SBP decreases, after which the HR decreases

302 and the SBP increases with a slight rebound bradycardia occurring with a nadir at 3-4 minutes
303 post oxytocin. Thomas et al. [5] injected a 5 U IV bolus as quick as possible and Moertl et al.
304 [9] during 10 seconds, which might maximize the cardiovascular effects.

305 The maternal hemodynamic effects apparently depend on the oxytocin injection time: when
306 given as a *statim* bolus of 5 IU oxytocin the peak effects on BP and HR occur within 30-60
307 seconds,[1,5,9] but when the same dose is given as an infusion over 5 minutes the effects are
308 blunted with no biphasic effect curve. [5] It is also clear that the hemodynamic effects depend
309 on the oxytocin dose: Sartain et al. [15] found less hemodynamic effects of a 2 IU oxytocin
310 bolus compared with a 5 IU bolus when injected over 5-10 seconds, and Jonsson et al. [8]
311 made the same experience when comparing 5 and 10 IU doses injected during one minute,
312 with peak hemodynamic effects after two minutes.

313 The different doses of oxytocin used and the different injections times explain the
314 inconsistency in the literature concerning the half-life as well as the peak effect of IV
315 oxytocin. The pharmacokinetics of oxytocin in pregnant baboons has been explained by
316 Kowalski et al. [27] using a two-compartment model, with a redistribution phase half-life of
317 1.1-1.7 minute and an elimination phase half-life of 8.0-9.6 minutes. To add to the
318 complexity, the two-compartment model seems to be valid only with high doses ($>0.5 \mu\text{g}/\text{kg}$),
319 but at lower doses the pharmacokinetics is described with a one-compartment model.[28]

320 Given these pharmacokinetic data, and adding the results from the studies by Thomas et al.
321 [5] and Jonsson et al. [8] and considering patient safety, we gave the oxytocin bolus during 60
322 seconds, assuming a delayed and blunted peak effect. The DPA recording at time point T3
323 began 60 seconds after the last drop of oxytocin and lasted for a good minute; thus, it is
324 possible that our T3 measurement covered parts of both the initial and the rebound phases.

325

326 It is well known that the chest discomfort some women experience during a CS is related to
327 the dose and speed of oxytocin injection.[5,15] The adverse hemodynamic effects of oxytocin
328 are added to the already present extensive adverse effects of spinal anesthesia, with global
329 vasodilation, fall in BP and cardiac affection, as demonstrated in the present study (Figure 1).
330 In the perspective of our findings, we believe it is wise to administer even a small bolus like 5
331 IU over a longer time than the minute used in the present study, particularly in women
332 showing circulatory instability. Furthermore, efforts should be made to enhance the spinal
333 anesthesia procedure in order to reduce the adverse circulatory effects. Spinal anesthesia with
334 concomitant procedures carries a risk also for the fetus.[29]

335 Apart from a decline in HR after oxytocin, our results generally support the findings in
336 previous studies. However, our study is the first to use the DPA technology and to show that
337 oxytocin causes vasodilation in large as well as in small and peripheral arteries. Since the
338 DPA is non-invasive, simple to use and the recording time is only about one minute, it is well
339 suited for pharmacological research and for screening. A disadvantage is that the method is
340 sensitive to body movements and cold fingers.[14,30,31] Other methods for PW analysis, like
341 applanation tonometry and oscillometry, are too slow to catch the rapid hemodynamic
342 responses to vasoactive drugs like oxytocin.

343 ***Weaknesses and strengths***

344 The complex interaction of hemodynamic events makes it difficult to selectively analyze the
345 effects of the individual procedures during a CS. A weakness is that the study series was
346 relatively small, comprising less than 20 paired observations for some of the statistical
347 analyses. Small series is a common problem in clinical experimental research, though our

348 sample sizes were in only two paired comparisons below the recommended threshold for
349 using the Wilcoxon matched-pairs signed-rank test.[32] This is a non-parametric statistical
350 tests, which then is more robust than its parametric equivalent, the paired t -test. Furthermore,
351 to evaluate the risk of type I errors we also tested with the Friedman non-parametric one-way
352 ANOVA for repeated measurements and performed Holm-Bonferroni adjustments of p
353 values. The strengths of the study are the novelty of digital photoplethysmography for pulse
354 wave analysis, a hitherto not explored method to study arterial stiffness in obstetrics, and the
355 longitudinal analyses of circulatory events occurring during the different steps of the CS
356 procedure.

357

358 ***Summary***

359 Both spinal anesthesia and oxytocin 5 IU IV bolus gave rise to profound maternal circulatory
360 effects, mainly arterial vasodilation and cardiac affection with ST index changes. Contrary to
361 previous studies, oxytocin resulted in a decrease in HR, suggesting a direct negative
362 chronotropic effect. The DPA parameters implied that oxytocin within minutes results in
363 vasodilation in both large and small arteries and increased LV ejection power. Cesarean
364 surgery and delivery of the baby resulted in a global increase in vascular tone and increases in
365 SBP and HR, suggesting momentous circulatory effects by these procedures. We believe
366 these seemingly contradictory changes can be a combined effect of maternal emotions and
367 auto-transfusion of blood from the empty and reduced uterus.

368

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371 Region Skåne.

372

373 **Disclosure of interest**

374 The authors declare no conflicts of interest

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376 **Geolocation**

377 Lund University and Skåne University Hospital, Lund and Malmö, Sweden

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477

478 Legend to figure

479 Box plots showing sequential changes in maternal mean arterial blood pressure (MAP), heart
480 rate, ECG ST index, ejection elasticity index, dicrotic index and pulse height from before
481 spinal anesthesia (point T0), after spinal anesthesia but before surgery (T1), after delivery of
482 the baby but before oxytocin injection (T2), 1 minute after IV oxytocin (T3), and 5 minutes
483 after oxytocin (T4). Arrows denote significant changes (Wilcoxon matched-pairs signed-rank
484 test, $p < 0.05$; within brackets $p < 0.10$ but ≥ 0.05) and direction of change. Figures denote
485 number of women in paired comparisons.

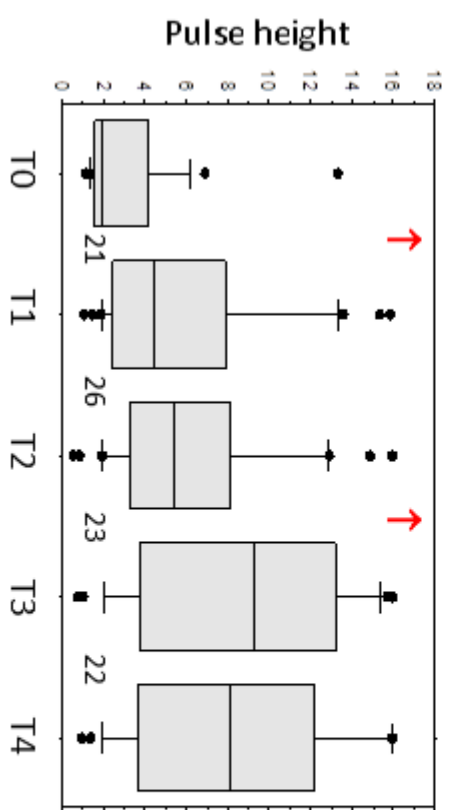
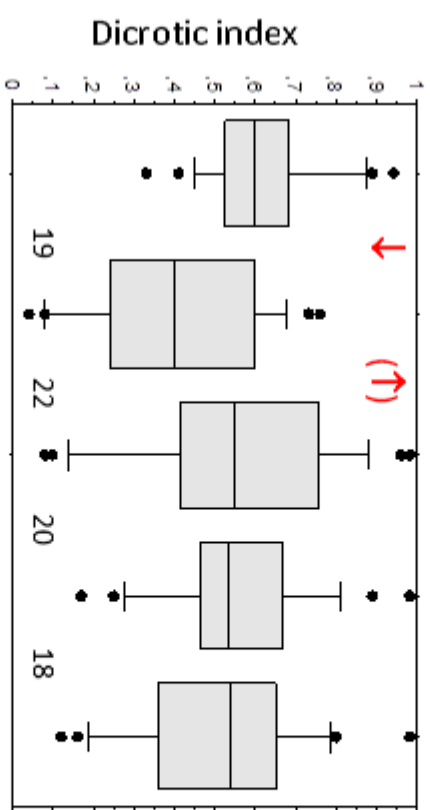
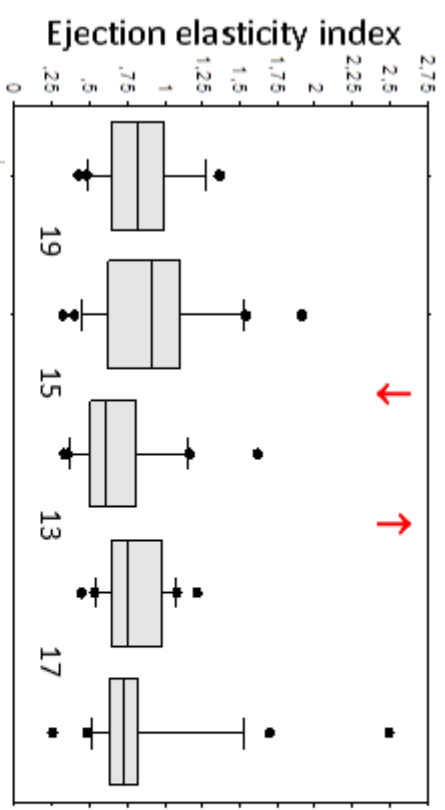
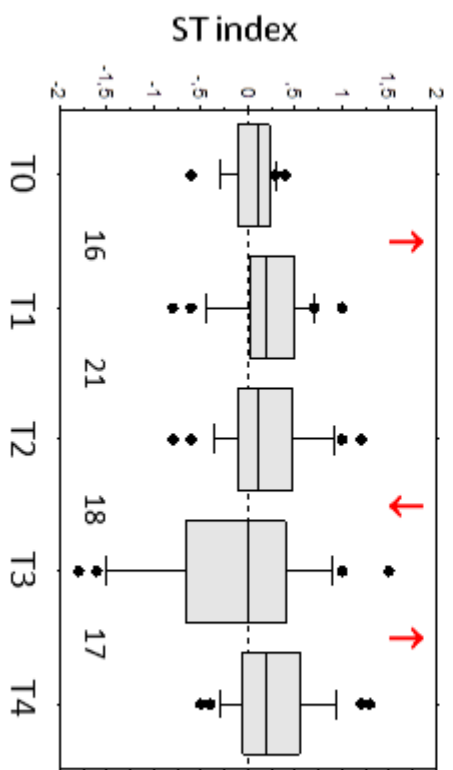
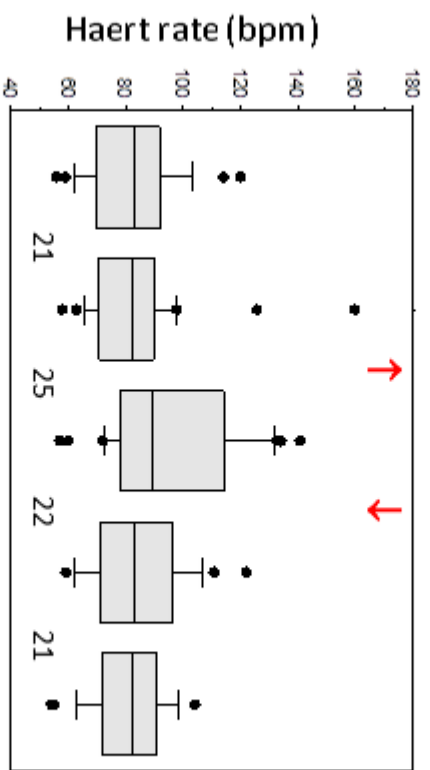
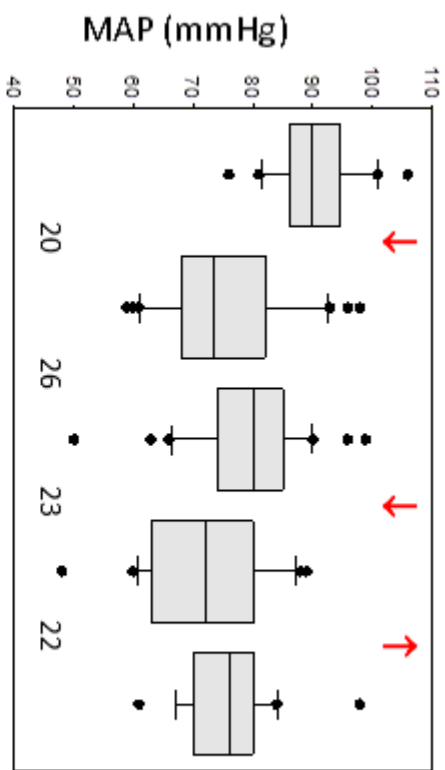


Table 1.

Description of the digital pulse wave analysis parameters used in the study (for detailed description, see [11]).

Parameter	Physiological background	Conditions with high values	Conditions with low values	Interpretation of increase	Interpretation of decrease
Pulse height (PH)	Circulation in small finger arteries, perfusion of finger tips	High BP, hyperthyroidism, fever, anemia, excessive blood volume, exercise, well-tuned athlete	Peripheral vasoconstriction, low BP, hypovolemia/dehydration, hypothyroidism, increased peripheral resistance	Peripheral vasodilatation	Peripheral vasoconstriction
Left ventricular ejection time compensated (ETc)	Represents systole, i.e. time from onset of the systolic upstroke limb to the closure of the aortic valve	Aortic valve stenosis, heart insufficiency, impaired CO, decreased large artery compliance (high vascular tone)	Hyperthyroidism, diastolic hypertension, small LV, decreased preload	Increase in LV ejection time, decrease in CO, increase in large artery vascular tone	Decrease in LV ejection time, increase in CO, decrease in large artery vascular tone
Cardiac ejection elasticity index (EEI)	Index for LV ejection capacity and compliance/elasticity of large arteries	Large-artery vasodilatation, anemia, increased LV ejection power, hyperthyroidism, congested heart failure	Large-artery vasoconstriction, arteriosclerosis, LV ejection insufficiency	Increase in LV ejection power, large-artery vasodilatation	Decrease in LV ejection power, large-artery vasoconstriction
Dicrotic index (DI)	Represents the peripheral circulation, indicates peripheral resistance	Small-artery vasoconstriction	Small-artery vasodilatation	Peripheral vasoconstriction	Peripheral vasodilatation
Dicrotic dilatation index (DDI)	$DDI = 1 - DI$. Index for elasticity in small	Small-artery vasodilatation	Small-artery vasoconstriction,	Small-artery vasodilatation	Small-artery vasoconstriction

	arteries		atherosclerosis		
<i>b/a</i>	Early systolic PW peaks identified by second derivatives of the crude PW curve contour; indicates LV ejection capacity and large-artery compliance/elasticity	Low large-artery elasticity, increased cardiovascular risk, vasoconstriction, atherosclerosis, increases by age	Young persons, athletes	Large-artery vasoconstriction, decreased LV ejection	Large-artery vasodilatation, increased LV ejection
<i>d/a</i>	<i>d</i> is a late systolic PW peak identified by derivative of the crude PW curve contour; mainly reflects the intensity of the tidal PW from small peripheral arteries	High small-artery elasticity, young persons	A longer negative <i>d</i> peak develops by advancing age, indicating arterial stiffness, atherosclerosis	Small-artery vasodilatation	Small-artery vasoconstriction
Ageing index (AI)	$AI = (b-c-d-e)/a$, representing the global vascular stiffness, i.e. "vascular age"	Atherosclerosis, increases by age	Young persons, athletes	Global arterial vasoconstriction	Global arterial vasodilatation

BP, blood pressure; CO, cardiac output; LV, left heart ventricle; PW, pulse wave

Table 2. Hemodynamic effects of spinal anesthesia and delivery of the baby at cesarean section. Figures are *p* values and arrows indicate a significant increase or decrease of parameter values; arrows within brackets denote a *p* value ≥ 0.05 but < 0.1 .

Parameter	Effects of spinal anesthesia		Effects of delivery	
	Wilcoxon test ^a T0-T1 ^b	Interpretation	Wilcoxon test ^a T1-T2 ^b	Interpretation
Systolic BP	↓ <0.0002	SBP decrease	↑ 0.025	SBP increase
Diastolic BP	↓ 0.0004	DBP decrease	0.70	No change
MAP	↓ 0.0003	MAP decrease	0.20	No change
Heart rate (HR)	0.53	No change	↑ 0.031	HR increase
ST index	↑ 0.028	ST increase	0.74	No change
PH	↑ 0.0057	Fingertip hyperemia as a sign of peripheral vasodilatation	0.20	No change
ETc	↑ 0.028	Increase in LV ejection time, decrease in CO, and/or large-artery vasoconstriction	0.94	No change
EEl	0.73	No change	0.12	No change
EEl@75 ^c	-	Not calculated because HR was unchanged	↓ 0.041	Large-artery constriction, decrease in LV ejection power
DI	↓ 0.0066	Small-artery vasodilation	(↑) 0.062	Marginal small-artery vasoconstriction
DDI	↑ 0.0066	Small-artery vasodilation	0.31	No change
DDI@75 ^c	-	Not calculated because HR was unchanged	↓ 0.16	No change
<i>b/a</i>	0.22	No change	↑ 0.045	Large-artery vasoconstriction decrease in LV ejection
<i>d/a</i>	0.38	No change	0.50	No change
AI	0.14	No change	↑ 0.003	Global arterial vasoconstriction

BP, blood pressure; MAP, mean arterial blood pressure; ST index, changes of the ECG ST segment; LV, left heart ventricle; CO, cardiac output

a) Wilcoxon signed-rank matched-pairs test.

b) For explanation of measurement points T0, T1 and T2, see text.

c) EEl and DDI, but no other parameters, were correlated with HR at T0; HR-adjustments to HR 75 bpm are denoted EEl@75 and DDI@75.

Table 3.

Hemodynamic effects of oxytocin administration (T2 to T4) during cesarean section. Figures are *p* values and arrows denote a significant increase or decrease of the parameter; arrows within brackets denote a *p* value ≥ 0.05 but < 0.1 .

Parameter	Effects of oxytocin				
	Wilcoxon signed-rank test			Interpretation	Friedman test T2-T3-T4
	T2-T3	T3-T4	T2-T4		
Systolic BP	0.38	0.31	0.74	No change No change No change	0.35
Diastolic BP	↓ 0.0162 ^a	↑ 0.024 ^a	0.45	Diastolic BP decrease Diastolic BP increase, restitution Back to T2 level at T4	0.019
Mean arterial pressure (MAP)	↓ 0.018	↑ 0.030	0.20	MAP decrease MAP increase, restitution Back to T2 level at T4	0.050
Heart rate	↓ 0.012 ^a	0.10	↓ 0.002 ^a	Heart rate decrease No change Heart rate decrease, occurred T2-T3	0.003
ST index	↓ 0.026	↑ 0.002 ^a	0.31	ST decrease ST increase, restitution Back to T2 level at T4	0.016
PH	↑ <0.001 ^a	0.31	↑ 0.020 ^a	Fingertip hyperemia No change Hyperemia, occurred T2-T3	0.0001
ETc	0.33	0.18	0.68	No change No change No change	0.45
EEI	(↑) 0.059	0.99	0.30	(Large-artery dilatation, ↑ LV ejection power) No change No change	0.20
EEI@75 ^b	↑ 0.028 ^a	0.70	0.12	Large-artery dilatation, ↑ LV ejection power No change No change	0.058
DI	0.85	0.99	0.80	No change No change No change	0.92
DDI	0.64	0.39	0.55	No change No change No change	0.93
DDI@75 ^b	0.20	0.37	0.64	No change No change No change	0.15
<i>b/a</i>	0.25	0.52	0.73	No change No change No change	0.70

<i>d/a</i>	0.86	↑ 0.033	↑ 0.018	No change Small-artery vasodilation Small-artery vasodilation, occurred T3-T4	0.053
AI	0.98	↓ 0.039	↓ 0.030	No change Global arterial vasodilation Global arterial vasodilation	0.16

- a) *p* value significant after Holm-Bonferroni adjustments (see text).
- b) EEI and DDI were the only parameters that significantly correlated with HR and were adjusted to a HR of 75 bpm.