Ordinal scale data were summarised with median and range and analysed using the Mann–Whitney *U* test and corrected for repeated measurements with Bonferroni–Holm correction. The immunological data were analysed by analysis of variances for repeated measurements as a general linear model. Log transformation was used if needed because of skewed distributions. All analyses used SPSS version 17.0 (SPSS Inc., Chicago, Illinois, USA). A *P* value of less than 0.05 was considered to be statistically significant.

We found no statistically significant differences in NK-cell cytotoxicity expressed in percentage between Groups P and E over time ($P = 0.54$ at 24 h and $P = 0.41$ at 72 h). The variation of NK-cell cytotoxicity in Group C (unoperated) was 1.6 (0 to 37.7), 6.5 (0.70 to 16.91) and 8.2 (2.15 to 32.7) preoperatively and at 24 and 72 h, respectively, postoperatively. The reactivity of T-lymphocytes sub-populations did not show statistically significant differences between Groups P and E at any time point (T-helper $CD4^+$, $P = 0.54$; T-cytotoxic $CD8^+$, $P = 0.72$). The $CD4^+/CD8^+$ ratio remained constant between the groups over time ($P = 0.99$). We observed a better preserved cytotoxic T-lymphocyte population in Group E and T-helper lymphocytes in Group P, postoperatively. After mitogen stimulation with phyto-haemoagglutinin, neither the cytotoxic lymphocytes nor the T-helper sub-population differed significantly between the groups at any measured times (Table 1). No statistically significant differences were seen in the ratio of IFN-γ/IL-10 ($P = 0.28$) or in VEGF ($P = 0.17$) between the groups at all the time points. There may be some explanations for our findings with respect to NK cells. First, patients in the epidural group also received inhalational anaesthetics, albeit in lower concentrations. It is also possible that the effects of anaesthetics on NK-cell cytotoxicity is minor compared with the effects of surgery per-se. Finally, there is a large intra-individual as well as inter-individual variation in measuring NK-cell cytotoxicity, which was confirmed in the control group of healthy individuals. Previous studies have focused on the effect of the anaesthetic technique on immune modulation with varying results.[6,7] In contrast to these studies including patients undergoing different types of surgery, we studied a homogenous population of patients scheduled for open radical prostatectomy under controlled conditions.

There are several limitations to the study: we did not define a primary outcome and therefore we did not perform power analysis. There is a lack of long-term data collection regarding cancer remission, allowing a possible correlation between the clinical impact and the immunological modulation, despite the small number of patients studied. In addition, our results are applicable only to patients undergoing radical prostatectomy for prostate cancer and for the specific method we used to assess NK-cell toxicity that has been previously used and validated against Chromium-release assay.

In conclusion, we were unable to confirm our hypothesis that thoracic epidural anaesthesia and analgesia prevents inhibition of some components of the immune system, compared with intravenous opioid analgesia in a clinical setting.

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Intraoperative hypotension and change in estimated glomerular filtration rate after major abdominal surgery

A prospective observational study

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Editor,

A reduced renal blood flow because of intraoperative hypotension may contribute to acute kidney injury. Recently, two retrospective studies showed that

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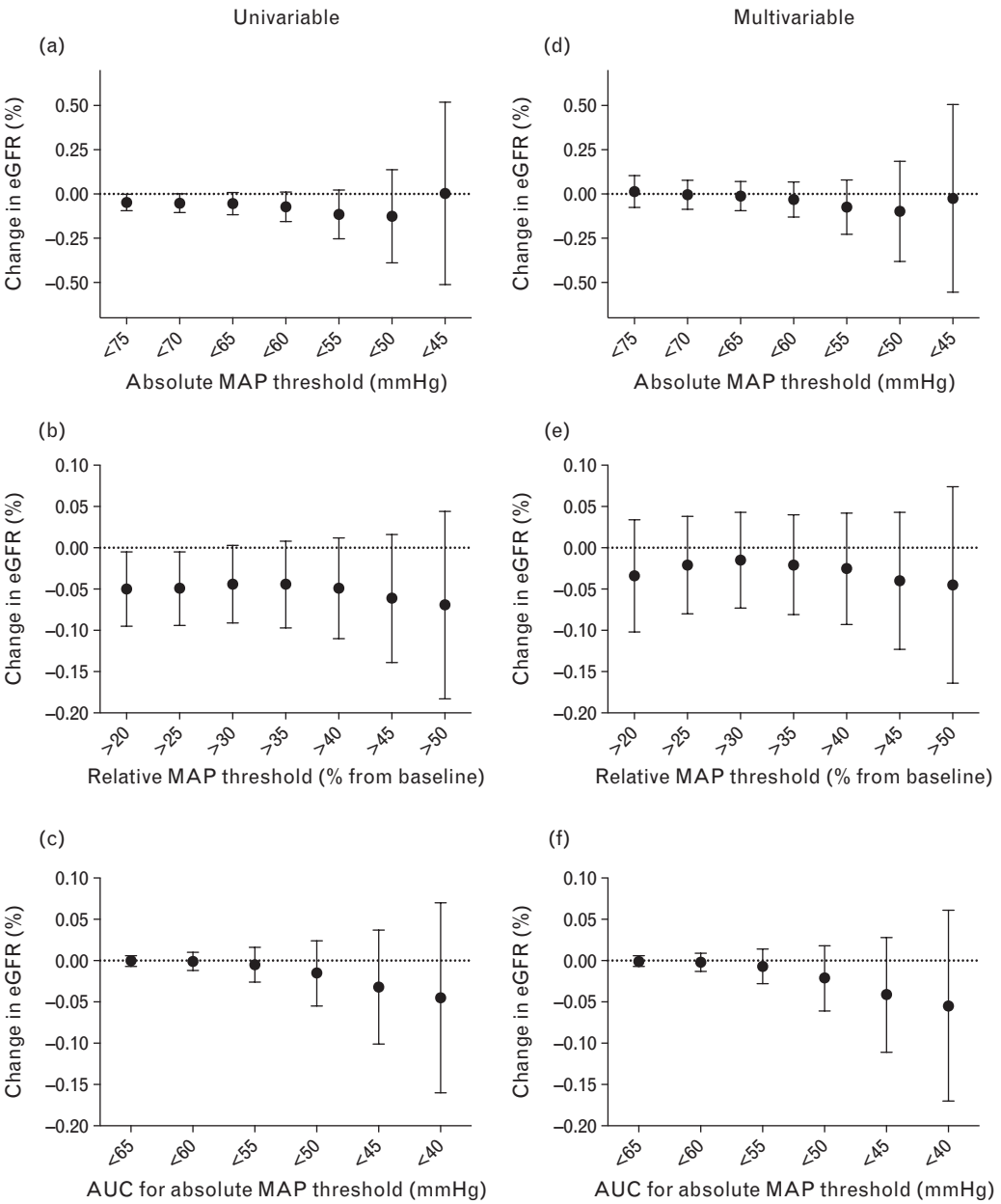
Fig. 1



Uni (a, b, c) and multivariable (d, e, f) analysis of absolute and relative MAP threshold values and AUC for MAP thresholds and change in eGFR. AUC, area under the curve; eGFR, estimated glomerular filtration; MAP, mean arterial pressure.

intraoperative hypotension was associated with an increased risk of acute kidney injury after noncardiac surgery.[1,2] Pre and postoperative serum creatinine values were not routinely measured, however, and this may have introduced bias. Also, the use of the estimated glomerular filtration (eGFR) rate may provide a more accurate assessment of renal function than serum creatinine.[3] The aim of this study was to determine whether intraoperative hypotension is associated with a change in eGFR in patients undergoing abdominal surgery with routine perioperative creatinine measurements.

The local Medical Research Ethics Committee (trial number W15.032) approved this secondary analysis of the prospective observational Myocardial Injury and Complications after major abdominal surgery (MICOLON) study (ClinicalTrials.gov Identifier NCT02150486). In the MICOLON study, the association between high-sensitive cardiac troponin T levels and noncardiac

complications after major abdominal surgery was investigated in patients at risk for coronary artery disease.[4]

Serum creatinine was routinely measured on the day of surgery and on the first, third and seventh postoperative day. eGFR was calculated using the Modification of Diet in Renal Disease 4 equation.[3] Primary outcome was change in eGFR, defined as the difference between baseline eGFR and lowest postoperative eGFR, expressed as a percentage of baseline eGFR value. In the sensitivity analysis we used the change in creatinine as the outcome variable.

Intraoperative hypotension was expressed as the total duration below several absolute and relative mean arterial pressure (MAP) threshold values and the area under the curve, combining depth and duration, for several MAP threshold values. MAP was recorded every minute in case of invasive blood pressure (BP) monitoring, and every 1 to 3 min in case of noninvasive monitoring. When the MAP was not measured or in case of an artefact, the prior MAP was carried forward to the next MAP measurement.

Linear regression analysis was used to assess the relation of intraoperative hypotension with change in eGFR, before and after adjustment for potential confounders. Potential confounders for the association of intraoperative hypotension and change in eGFR were age, sex, renin–angiotensin–aldosterone system inhibitors, congestive heart failure, American Society of Anesthesiologists classification, type of surgery, duration of surgery and blood loss.[2,5] Effect estimates are expressed as unstandardised coefficients (βs) with their accompanying 99% confidence interval (CI). As multiple thresholds are compared, we used a more stringent level of significance of $P < 0.01$ and hence present effective estimates with 99% CIs. For statistical analyses IBM SPSS, Chicago, IL version *22* was used.

In total, 202 patients were included in the analysis. Creatinine was available in all 202 patients at baseline, and in 99% (201/202), 96% (181/188) and 88% (106/121) of hospitalised patients on the first, third and seventh postoperative day, respectively. Invasive BP monitoring was performed in 120 patients (59%). In the univariable analysis, intraoperative hypotension, defined as a MAP below 75 mmHg, was associated with a change in eGFR (eGFR decreased with 0.05% for each minute spent below a MAP of 75 mmHg, 99% CI: −0.09 to −0.00, $P = 0.009$; Fig. 1a). A similar association was observed for intraoperative hypotension defined as a decrease in MAP of 20% (−0.05%, 99% CI: −0.10 to −0.01, $P = 0.004$) and 25% from baseline (−0.05%, 99% CI: −0.09 to −0.01, $P = 0.004$, Fig. 1b). The area under the curve for intraoperative hypotension thresholds was not associated with a change in eGFR (Fig. 1c). In the multivariable analysis, none of the intraoperative hypotension definitions were associated with change in eGFR (Fig. 1d, e and f). In the sensitivity analysis with a change in creatinine as the outcome variable, similar results were found.

The potential influence of intraoperative arterial perfusion pressure on organ function preservation is an ongoing debate. Walsh *et al.*[2] and Sun *et al.*[1] found, in two retrospective studies, that intraoperative hypotension, defined as a MAP below 55 mmHg, was associated with acute kidney injury. In contrast to these studies, we had highly detailed information on perioperative renal function for our study patients. Instead of using creatinine values that were requested by treating physicians on medical indication (potentially leading to confounding by indication and information bias), creatinine measurements were systematically conducted. In doing this, we may however, have missed the 'peak' creatinine value, potentially leading to an underestimation of the true incidence of acute kidney injury. We used eGFR as the outcome variable because it represents renal function better than creatinine.[3] A drawback of the eGFR, however, is that it has not been validated for patients with unstable creatinine values. However, the perioperative use of eGFR is recommended by others and the use of a change in creatinine as the outcome variable showed similar results.[6]

Typically, a decline in renal function is dichotomised at a creatinine level of 1.5 to 1.9 times baseline or an increase of at least 0.3 mg dl^{-1} ($\geq$26.5 μmol l^{-1}). Although categorisation of continuous variables is often done to simplify statistical analysis, dichotomising a continuous variable increases the chance of a type 1 error ('false positive').[7] By including the outcome as a continuous variable we increased statistical power to detect a true association. Still, our study may be underpowered to find an association between intraoperative hypotension and change in eGFR. For example, the change in eGFR we found in patients with MAP less than 55 mmHg (−0.074% for each minute below this threshold, 99% CI: −0.228 to 0.079) would have required the inclusion of 876 patients to reach statistical significance. A closer investigation of the effect estimates suggests a trend towards renal injury as BP declines, which may become statistically significant in larger sample sizes.

In summary, we did not observe an association between intraoperative hypotension and change in eGFR, although we cannot exclude that our study was underpowered. Nevertheless, the effect estimates of change in eGFR per minute intraoperative hypotension had not been studied before and could serve as a basis for sample size calculations in future studies.

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Personal electronic device use in the operating room

A survey of usage patterns, risks and benefits

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Editor,

Distraction in the operating room poses significant risks to patient safety. Vigilance has been the cornerstone of the well tolerated practice of anaesthesiology since its inception, and improvements in technologies allowing for enhanced vigilance have resulted in a tremendous reduction in anaesthesia-related morbidity and mortality. As technologies have become more complex and numerous, however, the risk of distraction has grown.[1,2] Over the past decade, the pervasiveness of personal electronic devices (PEDs) has led to a new form of distraction, as anaesthesia providers use these devices for both professional and personal purposes during patient care. A 2011 article in the New York Times coined the term 'distracted doctoring' and focused attention on this growing potential problem.[3]

Study of texting-while-driving behaviour suggests that PED-use can have an addictive component.[4] CAGE questionnaires have been used successfully to gauge levels of addiction in those abusing alcohol or participating in other potentially addictive behaviours.[5] We therefore designed a survey to assess anaesthesia provider opinion on PEDs and gauge self-reported level of device use via a previously described modified CAGE questionnaire. Ethical approval for this study (Human Investigation Committee protocol number 2014-348) was provided by the Human Investigation Committee of Beaumont Hospital, Royal Oak, Michigan USA (Chairperson John M. Koerber) on 8 January 2015, after which, a nine-question assessment tool was distributed to anaesthesiologists, residents and CRNAs, through the Association of Anaesthesiology Core Program Directors listserver. Questions included demographic assessment of level of training, availability of wireless internet access in the operating theatre, availability of wired or wireless internet access at the anaesthesia work station, a modified CAGE questionnaire (below) and a final question assessing risk/benefit analysis of PED use in the operating theatre.

Modified CAGE (m-CAGE) Questionnaire

	Question	Points
C	Have you ever felt you needed to **C**ut down on the use of your electronic device?	1
A	Has anyone ever **A**nnoyed you by criticising the use of your electronic device?	1
G	Do you ever feel **G**uilty about your electronic device use?	1
E	Do you reach for your electronic device as soon as you wake up (Eye-opener)?	1

Used to identify very high users of electronic devices (2 or more points) who may be targeted for additional help with prevention of distraction from electronic device use in OR.
Adapted from Papadakos.[6]

Six hundred and forty-seven respondents completed the assessment tool. Nearly all respondents had wireless internet access in the operating room (611/96%) and wired or wireless access at the anaesthesia work station (604/95%). Fifteen percent reported that their institution had specific PED policies in place, while 51% did not know. One hundred and thirty-three (21%) reported at least two risks on the m-CAGE questionnaire. Of those with positive m-CAGE screens, most had positive responses to two questions (63%), 28% had three positive responses and 9% of all respondents answered 'yes' to all four CAGE questions. Nearly all respondents felt that the benefits of PED use somewhat outweigh the risks (average 2.43 ± 1.11 on a 5-point Likert scale).

This survey included the use of a modified CAGE questionnaire. The CAGE questionnaire was initially developed by Ewing over 50 years ago[5] for use by primary care physicians as a convenient screening tool for alcohol addiction. The questionnaire has since been validated several times in different populations and has been used to screen for drug use, gambling, tanning and other compulsive behaviours.[7] Since 2013, a group at the University of Rochester has used a modified version of the questionnaire to help educate professional groups on