with the laparoscopic, but exclude the group that was converted from laparoscopic to open surgery, the blood loss was 387 ml (so 441) vs 116 ml (so 285), P=0.00006. The latter is of cause misleading because the patients who had invasive tumours difficult to remove or bleeding problems were converted to open surgery and thus excluded from the laparoscopic group.

Dr Salzwedel and Dr Reuter suggest that the evaporative loss is much smaller during laparoscopic surgery. This is in my opinion a very common claim which is not supported by evidence. The fact is that the abdomen is insufflated with dry air (CO₂), and both the abdominal wall and the inner organs are fully exposed. Furthermore, the air is replaced an unknown number of times during surgery. However, the actual evaporative loss has never actually been measured. On the other hand, the loss during open surgery is very small ranging from 8 to 32 ml h⁻¹ (note: strictly per hour, not per kilogram), the latter with completely opened abdomen and exteriorized intestines. Nevertheless, for the above reasons and other possible differences between open and laparoscopic surgery, we chose to stratify the randomization for the surgical method. The stratification worked well with absolutely no difference between the two groups compared.

Dr Salzwedel and Dr Reuter call for information on blood loss in our trial. We are most happy to provide the data: the intraoperative blood loss was: in the zero-balance group: mean 375 ml, so 402 (range 0–7000) vs the Doppler group: mean 297 ml, so 402 (range 0–1600); P=0.49. As seen, the replacement of lost blood in the zero-balance group with a mean of 475 ml Voluven reflects in my opinion great care from the team, and can hardly be done more accurate in daily clinical practice.

In my opinion, the most important finding in our trial is our very low complication rate. Even though one-third of the patients had rectal surgery, our anastomotic leakage rate was very low complication rate. Even though one-third of the patients had rectal surgery, our anastomotic leakage rate was very low. After a thoracic CT scan to exclude an aortic aneurysm, the patient was drowsy and hypotensive despite fluid administration, and hypovolaemia, it is possible to minimize the number of postoperative complications, and improve the outcome of elective colorectal surgery.

Declarations of interest

None declared.

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Levosimendan in a case of severe peri-myocarditis associated with influenza A/H1N1 virus

Editor—Pandemic influenza A/H1N1 spread worldwide in 2009–2010, but several new cases have been identified in 2011 in Italy. Respiratory failure requiring mechanical ventilation was the hallmark described during the influenza A/H1N1 pandemic and the patients with myocarditis were rare.¹² We report the case of a fulminant peri-myocarditis associated with influenza A/H1N1 virus that was successfully managed with levosimendan.

A 54-yr-old female with case history of mild hypothyroidism developed flu with fever, cough, and weakness. Two days later, the fever disappeared but she was brought to the emergency department (ED) of our hospital because of severe constrictive thoracic pain and fainting. At ED admission, the patient was drowsy and hypotensive despite fluid infusion (crystalloids 1.5 litre). Electrocardiography showed sinus tachycardia, low-voltage QRS with inferior and septal ST elevation; cardiac troponin I (Tn) was 1.4 ng ml⁻¹ and procalcitonin (PCT) 0.37 ng ml⁻¹. Trans-thoracic echocardiogram (TTE) showed a global depressed left ventricular function (ejection fraction (EF) 35%) and mild pericardial effusion. After a thoracic CT scan to exclude an aortic aneurysm, the patient was admitted to our intensive care unit (ICU) still hypotensive and anuric. Cardiac index (CI) and blood O₂ saturation in the superior cava vein (ScVO₂) were very low. After a further fluid challenge, we started dobutamine (up to 8 μg kg⁻¹ min⁻¹) but arterial pressure, CI, and ScVO₂ did not improve; serum lactate (La) and Tn increased to 5.5 mM and 3.9 ng ml⁻¹. Nasopharyngeal swab for reverse-transcriptase–polymerase-chain reaction (RT–PCR) test for the influenza A/H1N1 2009 virus resulted positive and, thereby, we started oseltamivir 150 mg twice daily and acetylsalicylic acid 3 g day⁻¹. The day after ICU admission, we performed cardiovascular magnetic resonance imaging that confirmed the diagnosis of severe peri-myocarditis (Fig. 1).

The persistence of hypotension and oliguria, associated with a mild pulmonary oedema and bilateral pleural effusion requiring non-invasive mechanical ventilation, led us to switch dobutamine to levosimendan (0.1 μg kg⁻¹ min⁻¹) before deciding on cardiovascular mechanical support. Twelve hours after levosimendan starting, CI increased, urine
output improved \( (0.8 \text{ ml}^{-1} \text{ kg}^{-1} \text{ h}^{-1}) \) and \( \text{La} \) decreased (3 mM). On ICU day 3, TTE revealed a significant improvement of EF (50%) and an increase in pericardial effusion. Tn increased to 11.2 ng \text{ ml}^{-1} \) and hypothesizing a persistence of A/H1N1 2009 virus, we performed a new RT–PCR test on nasal swab that was negative. In the following days, CI, \( \text{ScvO}_2 \), La, Tn, and urine output gradually improved and 6 days after ICU admission, the patient was transferred to the cardiac department and finally discharged home 12 days later with non-steroid anti-inflammatory drugs, diuretic, and \( \beta \)-blockers therapy.

Influenza A/H1N1 virus still caused death in Italy and worldwide in 2011, but the development of a peri-myocarditis associated with influenza A/H1N1 is still unusual. In our patient, the influenza A/H1N1 aetiology was likely because of clinical history, positive nasal swab RT–PCR test, and no identification of any other microbiological agents more commonly involved in severe peri-myocarditis.\(^3\) Patients' symptoms suggestive for cardiac disease during epidemic influenza must alert physicians on possible influenza A/H1N1 virus myocardial localization. Mechanical circulatory supports are reported as the main options to treat fulminant myocarditis in these patients.\(^4\) In our case, a less invasive treatment with non-invasive ventilation, non-steroid anti-inflammatory drugs, and levosimendan act as ‘bridge’ to aetiologic treatment with neuraminidase inhibitors. Moreover, in our patient, levosimendan may have played a cardioprotector role inhibiting apoptotic cell death and preventing cardiomyocyte loss, as previously reported in viral myocarditis in experimental models.\(^5\)\(^6\) Therefore, we believe that levosimendan can be considered as a therapeutic option in severe viral peri-myocarditis before the use of invasive mechanical circulatory supports.

**Declaration of interest**

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Do old pharmacokinetic parameter estimates predict new data?

Editor—Investigators may report different parameter estimates to describe the pharmacokinetics of a drug used in children. A number of parameter sets exist for describing propofol time–concentration data in children, often predicting quite different profiles in a typical child.1 These differences may be attributed to different patient populations, administration (single dose vs infusion), study duration, and differing analysis methodologies. Similarly, parameter sets for i.v. paracetamol are reported that differ.2 3

An alternative to comparing predicted time–concentration profiles using differing parameter sets for a typical child is to ascertain if parameter estimates from an earlier study can predict concentrations similar to those reported in a new study is to use a modelling tool known as the visual predictive check.4 Concentration prediction intervals from an earlier study5 are graphically superimposed on those intervals determined from observed concentrations in the new study.2 Simulation is performed with parameter estimates from the earlier study using 1000 subjects with characteristics taken from new patients. For data such as these where covariates such as dose, weight, and height are different for each patient, a prediction-corrected visual predictive check6 is used; observations and simulations are multiplied by the population baseline value divided by the individual-estimated baseline. Figure 1 shows a graphical representation. The median predictions and observations graphically lie on top of each other. Observed concentration intervals are narrower than predictions, reflecting limited subjects (n=33) in the new study.

The earlier study (n=144) was performed using a prodrug of paracetamol (procetamol) that is rapidly metabolized to paracetamol (F=0.5) by plasma esterases. This graphical validation supports parameter estimates for i.v. paracetamol determined using the prodrug.

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Fig 1. Prediction-corrected visual predictive check using parameter estimates from an earlier study5 and observations from the new study.2 All plots show the median and 90% intervals (solid and dashed lines). (a) shows all prediction-corrected observed concentrations. (a) shows prediction corrected percentiles (10%, 50%, and 90%) for observations (lines with symbols) and predictions (lines) with 95% confidence intervals for prediction percentiles (green-shaded areas).