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# Letter to the Editor

## HIPEC and the necessary hyperthermia: do we still need the open abdomen?

*Dear Editor,*

I read with interest the article by Di Miceli et al[1] entitled "Complications related to hyperthermia during hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC) treatment. Do they exist?".

The Authors performed a Medline search on bowel perforation and fistula occurring postoperatively after HIPEC. They chose to focus their attention on those studies[2-5] that used the open-abdomen HIPEC technique, and I agree with their belief that the risk of scald injuries to the bowel is not a prerogative of the closed-abdomen technique.

The improved distribution of heat and the reduced risk of thermal injuries are credited to the Coliseum technique according to Elias et al[4] and Stephens et al[5]. However, the evidence resulting from those two studies should be called into question.

Elias et al[4] described their experience with 7 different techniques of intraperitoneal chemotherapy that they tested in 32 patients: each technique was tested in a very small number of patients (average 4 to 5 patients). As far as Statistics and sample size calculation are concerned, only huge differences between techniques are expected to be significant with such small samples. When sample size is not adequate, the differences found are insignificant, and care must be taken not to draw any inferences from them. Therefore, one can argue that, in the study by Elias et al, the claimed superiority of the open-abdomen technique cannot be considered evidence-based but rather a conclusion based on the opinion of the Authors.

Stephens et al[5] reported their experience with 200 treatments, administered to 183 patients by means of their newly developed Coliseum technique. When discussing their results in terms of improved heat distribution and reduced risk of thermal injury with the Coliseum technique, their conclusion is merely based on the fact that they did not observe an increased occurrence of fistula despite higher temperatures of the inflowing perfusion fluid. Indeed, one can reasonably argue that this is just an arbitrary assertion and not a demonstration. In fact, the Authors used only two thermal probes and did not perform any measurement to demonstrate that the temperature across the entire abdominal cavity was homogeneous. Moreover, their study was not designed to compare the Coliseum technique with the closed-abdomen technique, but was simply an observational study.

The true reality, which is clearly spotted by the results of the search performed by Di Miceli et al[1], is that no sound evidence can demonstrate that the distribution of heat is improved with the Coliseum technique. Moreover, when studies were performed using multiple thermal probes or thermographic images, a heterogeneous distribution of heat was found with the open-abdomen techniques, and some abdominal regions could never reach the desired temperature[6,7].

A homogeneous distribution of heat across the abdominal cavity is impossible with the Coliseum technique. The explanation for this inability comes from physics and is about the inevitable thermal gradient that is inherent with the architecture of the Coliseum.

In the Coliseum technique, a powerful thermal gradient is created between a broad cooling surface, i.e., the surface of the perfusion fluid that is at room temperature, and a very small

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heating area, i.e., the tip of the inflow catheter(s). This temperature gradient is maintained during the entire perfusion period by the constant supply of fresh air attracted by the smoke evacuator, which promotes a huge dissipation of heat by convection and evaporation. To compensate for this great heat dissipation, there is need to increase the flow rate and the temperature of the inflowing fluid, and the heating source is forced to work at full power, to deliver a huge amount of heat in a relatively small area: to maintain an average temperature of 41-42°C in the abdominal cavity an inflow rate of up to 1000 ml/min of fluid at 46 ± 0.5°C is often needed[8]. Therefore, close to the tip of the inflow catheter(s) the risk of scald injuries to the bowel is real.

The thermal gradient is the most powerful engine that moves the perfusion fluid during a Coliseum HIPEC. Hot fluid quickly moves upwards and reaches the surface of the basin where it is efficiently cooled; after cooling, the fluid moves to the bottom of the basin where it stagnates until it is kept by the outflow drains. An equilibrium is impossible, as long as the thermal gradient is maintained.

Several authors and the same proposers of the Coliseum technique state that the constant manipulation of the perfusate ensures a homogeneous distribution of the heated fluid within the peritoneal cavity[2,9]. The image of the Surgeon who acts with her/his hands to distribute heat and chemo is very powerful and is a suggestion that influenced many operators. Indeed, the belief that mixing the perfusate by hand entails the homogeneous distribution of heat is not supported by any evidence. Moreover, when it comes to physical laws, that claimed homogeneous distribution is very unlikely to occur.

We can take an example from industrial fluid mixers, which consist of a tank and an impeller. As the engineers who design fluid mixers know well, effective mixing requires the proper shape of the tank and the proper shape, positioning and rotational speed of the impeller[10,11]. When these requirements are not met, fluid stagnates at the bottom of the tank and is not mixed at all. We can easily observe that the abdomen is not a properly shaped tank (it is rather like a maze with multiple compartments) and that the hand is not a properly shaped impeller. With the wrong tank and the wrong impeller, effective fluid mixing is an illusion, and we should conclude that in the Coliseum technique the manipulation of the perfusate produces little if any modification in the distribution of heat across the abdominal cavity, especially at the bottom of the basin where the cooled fluid accumulates.

So, why should we leave the abdomen open during HIPEC and accept the unacceptable heat dissipation and thermal inefficiency of the Coliseum technique?

The sole evident advantage of the Coliseum technique over the closed-abdomen technique is the ability to displace the bowel and keep all the abdominal recesses open during the perfusion. Now, the same result can be achieved in a closed-abdomen by means of the Laparoscopy-Enhanced HIPEC technique (LE-HIPEC), which we described recently[12,13]. Moreover, according to our case load[14], the LE-HIPEC allows the detection and division of the early intra-abdominal adhesions that occur during the closed-abdomen perfusion period, thus keeping all the abdominal recesses accessible to the heated perfusion fluid and avoiding the onset of preferential flows[14-16].

As far as we are concerned, when considering the proper administration of hyperthermia as a necessary part of HIPEC, we should better become aware of the thermal gradient affair and contemplate giving the open-abdomen techniques up.

**Conflict of Interest**

The Authors declare that they have no conflict of interests.

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