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An inexact study design produced misleading conclusions: To perform operative procedures in an optimized local atmosphere: Can it reduce post-operative adhesion formation? de Vries A, Mårvik R, Kuhry E. [Int J Surg 2013 Sep 27. pii: S1743-9191(13)01053-4. doi: 10.1016/j.ijisu.2013.09.005]

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**TITLE PAGE**

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**MANUSCRIPT:**

Dear Sir,

Since adhesion formation pathogenesis has been our research interest for a long time we read with great interest a recently published article in your journal entitled “To perform operative procedures in an optimized local atmosphere: Can it reduce post-operative adhesion formation?” by de Vries et al.<sup>1</sup> The authors concluded that during surgery the rats exposed to the warmed and humidified artificial atmosphere consisting of more than 75% carbon dioxide and 3-4% oxygen had more severe and more post-operative adhesions compared to the rats that were exposed to the ambient air during surgery.

In our opinion technical factors highlighted by the authors<sup>1</sup> in discussion section may have been biased, the results were probably exaggerated and their conclusions therefore misleading. The design of this study<sup>1</sup> is not clear and is inexact due to differences in adhesion model creation modes which were done in different circumstances either inside of the Perspex box with limited space for surgeon's manipulations or in the ambient air without limitations for surgeon. Subsequently it is difficult to be sure of their conclusions.

In a series of experimental studies we have shown that CO<sub>2</sub> insufflation did not increase parameters of adhesion formation in comparison with those of open surgery<sup>2</sup> nor in an open laparoscopy model<sup>3</sup> with and without CO<sub>2</sub>-insufflation when surgical procedures were strictly standardized. Analogously the absence of any impact of CO<sub>2</sub>-insufflation/CO<sub>2</sub>-pneumoperitoneum or even its antiadhesiogenic properties has been demonstrated in many well-designed studies<sup>4-7</sup> with exploration of underlying pathways and pathophysiological mechanisms<sup>8-12</sup>. Moreover a crucial impact of surgical technique on adhesion formation was demonstrated in many studies with different modes of surgical trauma<sup>2,3,13-21</sup>.

We previously have discussed<sup>2,3,22,23</sup> methodological shortcomings with subsequent untenable conclusions of studies showing an impact of CO<sub>2</sub> insufflation/pneumoperitoneum with small-scale gas mixtures, in which were cited the authors in this article<sup>1</sup> whereas studies proving an opposite opinion were not cited at all. In such study with uncertain conclusions, the authors<sup>1</sup> should have discussed opposite positions. Therefore a well-designed study with standardized surgical procedures could cast light on the highly complex pathophysiology of adhesion formation and the impact of gas-environment on this process.

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