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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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EFFECT OF INHALED OXYGEN CONCENTRATION ON PULMONARY GAS EXCHANGE DURING OFF-PUMP CORONARY BYPASS GRAFTING

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Abstract.

Aim of study: Supra-physiologic level of PaO_2, securing oxygen reserves and preventing perioperative hypoxia, may offset the reduced oxygen delivery during cardiac surgery. However, high FiO_2 will speed up gas absorption in low V/Q regions, promote atelectasis formation and increase pulmonary shunt fraction. PaO_2/FiO_2, P(a-Et)CO_2 and $PEtCO_2/PaCO_2$ are the variable linked to CO_2 and O_2 exchange impairment. The aim of our study was to assess pulmonary gas exchange performance while ventilating patients with different FiO_2 during OPCABG.

Material and methods: The seventy patients were randomly equally distributed in two groups: H (High) and L (Low). The patients in the group H were ventilated with FiO_2 0.8 and the patients in the group L _ with FiO_2 0.5. PaO_2/FiO_2 ratio, P(a-Et) CO_2 gradient and $PEtCO_2/PaCO_2$ ratio were checked at the start and the end points of operations.

Results: PaO_2/FiO_2 decreased, P(a-Et)CO_2 increased and $PaCO_2/PEtCO_2$ decreased at the end of operations compared with the start values in both groups. PaO_2/FiO_2, P(a-Et)CO_2 and $PaCO_2/PEtCO_2$ ware different between H and L groups. The difference became statistically significant at the end of operations. (PaO_2/FiO_2 326±65 vs 290±63 p=0.020; P(a-Et)CO_2 5.7±2.3 mmHg vs 7.5±2.4 mmHg p=0.003; $PaCO_2/PEtCO_2$ 0.84±0.05 vs 0.80±0.06 p=0.001). The groups were comparable according to the outcomes such as hemodynamic and laboratory data, duration of postoperative mechanical ventilation and ICU length of stay.

Conclusions: FiO_2 0.8 was associated with more derangements of pulmonary gas exchange compared with FiO_2 0.5. Although FiO_2 did not have an impact on the outcomes we studied, using FiO_2 0.5 seems to be safer in patients undergoing OPCABG.

Key words. FiO_2, pulmonary gas exchange, anaesthesia, OPCABG.

Introduction.

Supplemental oxygen is conventionally employed to secure oxygen reserves and prevent perioperative hypoxia. Traditionally, high arterial partial pressures of oxygen (PaO_2) have been used to maximize tissue oxygen delivery during cardiac surgery [1]. Supra-physiologic level of PaO_2 increases the oxygen gradient between capillaries and peripheral tissue, which may offset the reduced oxygen delivery (DO_2) caused by hypothermia, fluid shift, myocardial dysfunction, blood loss, and anaemia during cardiac surgery [2]. DO_2, interrogated by SvO_2 (mixed venous oxygen saturation), may increase to a clinically significant degree as inhaled oxygen fraction (FiO_2) is increased during cardiac surgery, and the increase of SvO_2 is not related to Hb concentration [3]. In their study, Ju et al. [4] observed that a mild increase in intraoperative PaO_2 may result in improved survival after OPCABG.

The pros and cons of hyperoxia has been debated during many years. Several meta-analyses were done about this topic [5,6]. In 2018 was published World health organization (WHO) global guidelines for the prevention of surgical site infection (SSI) [7]. Guidelines development group suggests that adult patients undergoing general anaesthesia with tracheal intubation for surgical procedures should receive an 80% fraction of FiO_2 intraoperatively and, if feasible, in the immediate postoperative period for 2-6 hours to reduce the risk of SSI. Two systematic reviews were conducted [8,9]. In patients under general anaesthesia with endotracheal intubation and mechanical ventilation, 80% FiO_2 reduced the incidence of SSI. No evidence of harm with high FiO_2 was found for major adverse effects (atelectasis, cardiovascular events, intensive care admission, death during the trial) in the meta-analysis of randomized trials. According to the recent trial, perioperative hyperoxia therapy (FiO_2>0.8) with the aim of decreasing SSI did not increase cardiovascular complications after elective colorectal surgery in a general population [10].

Most anaesthetics cause a loss of muscle tone that is accompanied by a fall in the resting lung volume. The lowered lung volume promotes cyclic (tidal) or continuous airway closure. High inspired oxygen fractions cause rapid absorption of gas behind closed airways, resulting in atelectasis [11]. Overall, about 75% of impaired oxygenation can be explained by atelectasis and airway closure taken together [12]. 10-20% of the lung is regularly collapsed at the base of the lung during uneventful anaesthesia, before any surgery has been performed. After thoracic surgery and cardiopulmonary bypass, >50% of the lung can be collapsed still several hours after surgery [13,14].

Atelectasis causes a reduction in gas exchange capacity and leads to intrapulmonary right to left shunts [15], which can be assessed by a decrease in the ratio between the arterial oxygen tension and the inspired oxygen concentration, the oxygenation index (PaO_2/FiO_2) [16].

End-tidal PCO_2 ($PEtCO_2$) is routinely used in the clinical assessment of the adequacy of ventilation because it provides an estimate of $PaCO_2$. How well $PEtCO_2$ reflects $PaCO_2$ depends on the gradient between them, expressed as P(a-Et)CO_2. The major determinant of P(a-Et)CO_2 is alveolar dead space (VDalv). The alveolar dead space may be derived as follows: VDalv = (1 − $PEtCO_2$/ $PaCO_2$). As measured by this equation, VDalv depends both on the "true" alveolar dead space and on the extent of the

venous admixture, the $PEtCO_2/PaCO_2$ ratio may be seen as a direct overall meter of the gas exchanger performance in a scale from 0 to 1. The presence of alveolar dead space and/or venous admixture at different extent would progressively decrease this ratio from the unity, reflecting the progressive deterioration of gas exchanger in its two components, oxygenation, and CO_2 removal [17].

The aim of our study was to assess PaO_2/FiO_2 ratio, $P(a\text{-}Et)CO_2$ gradient and $PEtCO_2/PaCO_2$ ratio changing while ventilating patients with different FiO_2 during off-pump coronary artery grafting operations. We tried to answer the question, how higher FiO_2 could worsen pulmonary gas exchange during OPCABG and if it might have a significant effect on the outcomes such as hemodynamic and laboratory data, duration of postoperative mechanical ventilation and ICU length of stay.

Materials and Methods.

This study was approved by ethical review board of Tbilisi 5th clinical hospital in 2022 (# CS03-022). Informed consents were obtained from all individuals. The study was conducted from April 2022 to November 2022.

The seventy patients were randomly equally distributed in two parallel groups (H _ High and L _ Low) with 1:1 allocation ratio (35 patients in each). All of them underwent to OPCABG. The patients in the group H (high) were ventilated with FiO_2 0.8 and the patients in the group L (low) were ventilated with FiO_2 0.5.

Sample size was calculated at http://sample-size.net. We hypothesized that the mean gradient $P(a\text{-}Et)CO_2$ between $PaCO_2$ and $PEtCO_2$ would be greater in the group H, where patients received high oxygen concentration. The calculated sample was equal to 32 with α (two-tailed) =0.01, β =0.1 assuming effect size = 2 and Standard deviation = 2.

Randomization was done by online program "Research randomizer". (https://www.randomizer.org/).

Inclusion criterium to involve patients in our study was the European System for Cardiac Operative Risk Evaluation (EuroSCORE) II. To create homogenous group with relatively low preoperative risk, only "EuroScore < 5" patients were included. We used preoperative pulse oximetry (SpO_2) as exclusion criterium. Patient with arterial oxygen saturation less than 97% were excluded.

All patients received intravenous access and were induced with midazolam 2mg/kg, fentanyl 5mcg/kg and pancuronium 0.1 mg/kg. Intubation of trachea was performed following 5 minutes mask manual ventilation with FGF 6-8 L/min FiO_2 1.0. After the patient was intubated and airway secured, FGF was set at 2 L/min and the vaporizer opened fully at 8% for sevoflurane. The patients were ventilated with anaesthetic machine "Drager Primus" in VCV mode: Vt 8ml/kg, f 10-12/min, I:E 1:2, PEEP 3mbar. As soon as the anaesthetic concentration reached to 1.2 MAC, the vaporizer setting was adjusted to keep the concentration at 1.1-1.2 MAC during the operation. Fresh gas oxygen concentration ($F_{del}O_2$) was adjusted to keep inhaled oxygen concentration (FiO_2) about 0.5 in the group L and about 0.8 _ in the group H. We used fentanyl infusion 2mcg/kg/h for analgesia with intermittent boluses 1 mcg/kg as needed. We added pancuronium 0.01 mcg/kg in every hour after induction for muscle relaxation. Hemodynamic was stabilized by α- and β- mimetic and blocker agents. We used dobutamine and norepinephrine via infusion and metoprolol and urapidil via boluses as needed. Heart rate, invasive arterial pressure and central venous pressure data were recorded per five minutes. Either average or median values of hemodynamic data were calculated and compared between groups as well as the medications consumed during operation.

Arterial blood gas sampling was done mandatory after 30 minutes from the beginning of mechanical ventilation and at the end of the operation. $PEtCO_2$ was monitored by gas analyser of the anaesthesia machine "Drager primus". The $P(a\text{-}Et)CO_2$ gradient and $PEtCO_2/PaCO_2$ ratio were calculated at these two points. Arterial oxygen partial tension (PaO_2) was registered and PaO_2/FiO_2 ratio was calculated as well.

We evaluated blood lactate, creatinine, and cardiac troponin I levels. Blood sampling for lactate and creatinine was done after 30 minutes from tracheal intubation, at the end of the operation, on the first and the second postoperative morning. We evaluated cardiac troponin I level after 12 hours from the end of the operation.

Statistical analysis of acquired data was performed by the program IBM® SPSS® Statistics 23. According to exploring data distribution normality, values are presented either as mean and standard deviation or median with interquartile range. Comparison of normally distributed values were done by Student's t-test and paired t-test. Variables not following a normal distribution were compared by non-parametric tests (Mann-Whitney U test; Wilcoxon signed rank test). The Chi-Square test was used to examine whether or not two nominal (categorical) variables had a significant connection. All tests were two-tailed. A P-value < 0.05 was considered statistically significant.

Results.

The demographic data of the patients involved in H and L groups are shown in the Table 1.

The mean FiO_2 was about 50% in the group L and about 80% _ in the group H. The mean PaO_2 was significantly different between groups at both points of anesthesia (at 30 minutes passed after intubation and at the end of the operation). The mean PaO_2 as well as the mean PaO_2/FiO_2 ratio decreased at the end of operations compared with the start values in both H and L groups, but more intensively in the H group. (Table 2).

We used PaO_2/FiO_2 ratio as an indicator of oxygenation status. Its' mean value was slightly low in group H comparing with group L at 30 minutes passed after starting mechanical ventilation and the mean difference became statistically significant at the end of operations. (Figure 1).

$P(a\text{-}Et)CO_2$ gradient mean value increased and $PaCO_2/PEtCO_2$ decreased at the end of operations compared with the start values in both H and L groups. The difference of the mean values between start and end points were statistically significant in the group H (Table 3).

$P(a\text{-}Et)CO_2$ gradient mean values as well as $PaCO_2/PEtCO_2$ ratio were different between H and L groups. The difference became statistically significant at the end of operations (Figure 1).

FiO_2 level did not have an effect on the outcomes we studied. The H and L groups were similar according to the hemodynamic

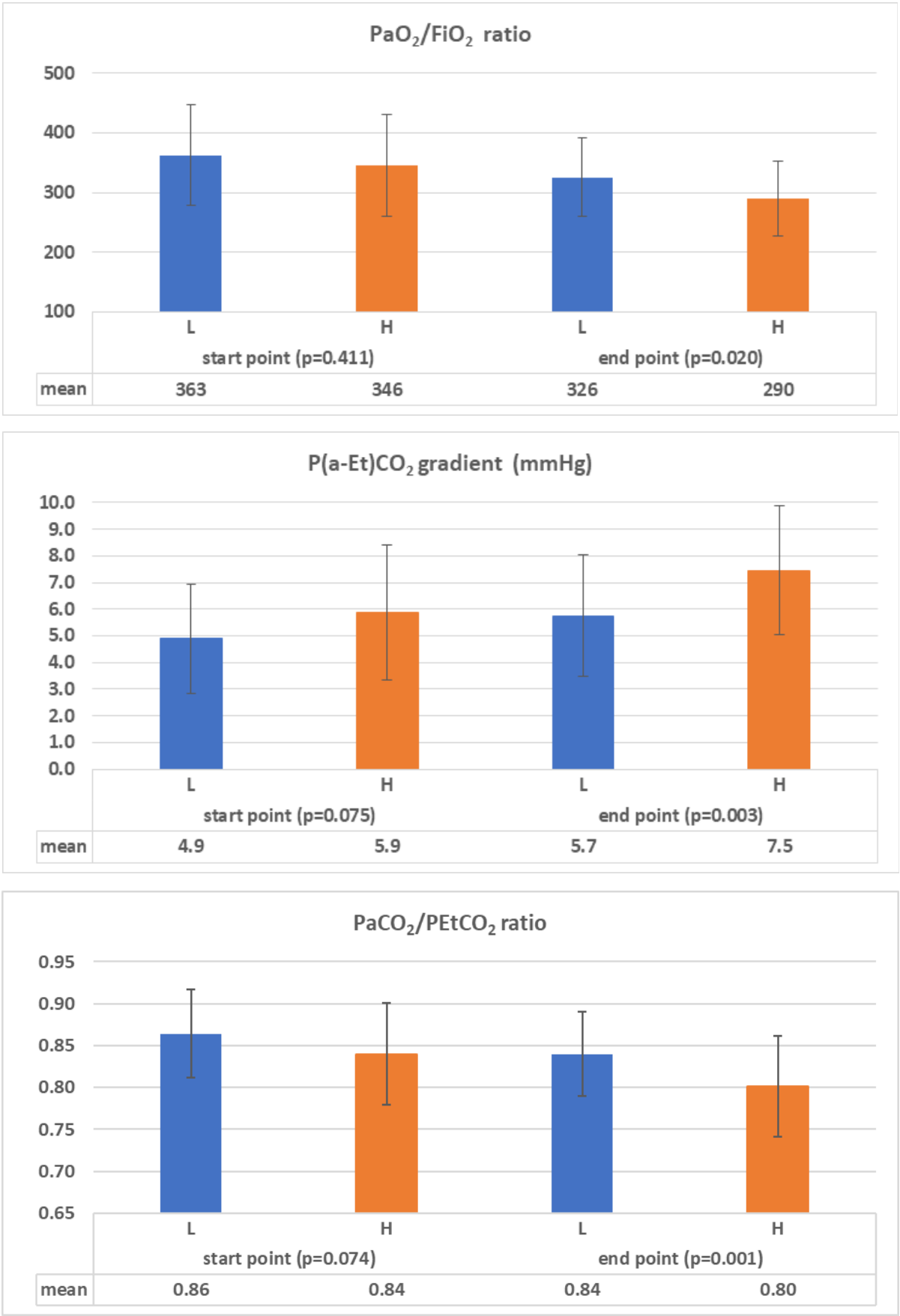

Figure 1. *Comparison of PaO_2/FiO_2 ratio, $P(a\text{-}Et)CO_2$ gradient and $PEtCO_2/PaCO_2$ ratio (mean ±SD) between L and H groups at the start and the end points of operations.*

Table 1. *Demographic data of the patients distributed into the L and the H groups.*

	L	*H*	
Age (y)	66.9 ± 8.0	67.3 ± 7.2	P = 0.814
Sex (F/M)	11 / 24	13 / 22	P = 0.802
Weight (kg)	79.6 ± 12.1	78.6±10.0	P = 0.712
BSA (m2)	1.91 ± 0.16	1.89 ± 0.13	P = 0.568

Table 2. *Comparison of PaO_2 and PaO_2/ FiO_2 ratio between L and H groups at the start and the end points.*

	L	**H**		**L**	**H**		**L**	**H**	
	FiO_2 (%)			**PaO_2 (mmHg)**			**PaO_2/FiO_2**		
At 30 min	50.1 ± 3.0	80.8 ± 2.2	P<0.001	181 ± 40	280 ± 70	P<0.001	363 ± 84	346 ± 85	P=0.411
At the end	49.6 ± 4.7	80.5 ± 2.0	P<0.001	161 ± 31	233 ± 66	P<0.001	326 ± 65	290 ± 63	P=0.020
	P=0.568	P=0.523		P=0.004	P=0.020		P=0.009	P=0.010	

Table 3. *Comparison of $P(a\text{-}Et)CO_2$ gradient and $PaCO_2/PEtCO_2$ ratio between the start and the end points in the H and L groups.*

	H			**L**		
	at 30 min	at the end		at 30 min	at the end	
$P(a\text{-}Et)CO_2$ (mmHg)	5.9 ± 2.5	7.5 ± 2.4	P=0.030	4.9 ± 2.1	5.7 ± 2.3	P=0.120
$PaCO_2/PEtCO_2$ ratio	0.84 ± 0.06	0.80 ± 0.06	P=0.025	0.86 ± 0.05	0.84 ± 0.05	P=0.136

Table 4. *Comparison of outcomes between the H and the L groups.*

	L	**H**	
Hemodynamic data			
HR (min^{-1})	76.3 ± 7.5	74.9 ± 7.7	P=0.424
MAP (mmHg)	76.5 ± 2.9	75.5 ± 2.5	P=0.221
Norepinephrine (mcg/kg/min)	0.04 [0.02; 0.06]	0.04 [0.03 0.09]	P=0.231
Urapidil (mg/kg)	0.06 [0.00; 0.20]	0.05 [0.00; 0.16]	P=0.445
Dobutamine (mcg/kg/min)	2.25 [1.77; 2.87]	2.15 [1.76; 2.85]	P=0.716
Metoprolol (mg/kg)	0.02 [0.00; 0.03]	0.02 [0.00; 0.04]	P=0.975
Laboratory data			
Peak Lactate (mmol/L) during 72 h	1.57 [1.30; 1.90]	1.50 [1.30; 1.80]	P=0.624
Creatinine increase (%) during 72 h	13.1 [8.0; 22.0]	14.0 [9.7; 28.6]	P=0.445
Cardiac Troponin I (ng/ml) after 12 h	0.140 [0.070; 0.350]	0.092 [0.068; 0.350]	P=0.593
ICU mechanical ventilation (hours)	8.0 ± 1.9	8.3 ± 2.0	P=0.561
ICU length of stay			
≤ 48 h	32 (91.4%)	30 (85.7%)	P=0.710
> 48 h	3 (8.6%)	5 (14.3%)	

and laboratory data. We did not find statistically significant difference between the H and L groups in the outcomes such as the duration of postoperative mechanical ventilation and the ICU length of stay (Table 4).

Discussion.

High FiO_2 may increase $P(a\text{-}Et)CO_2$ gradient by preferentially vasodilating well-perfused alveoli, resulting in the redistribution of blood flow to these alveoli from poorly perfused alveoli and an increase in VDalv. Larson and Severinghaus [18] reported that the administration of O_2 to awake sitting subjects led to an increase in $P(a\text{-}Et)CO_2$. They attributed this finding to the vasodilating effect of O_2 on blood vessels at the base of the lungs, which results in the expansion of the apical VDalv. The changes in $P(a\text{-}Et)CO_2$ are most likely due to the dilution effect of alveolar PCO_2 ($PACO_2$) with gas from VDalv.

Yamauchi H, et al. [19] demonstrated that $P(a\text{-}Et)CO_2$ depends on FiO_2 in anaesthetized ventilated patients. They concluded, that not only the true VDalv but also intrapulmonary shunt and cardiac output may be associated with the magnitude of $P(a\text{-}Et)CO_2$ in the presence of variable FiO_2.

A major cause for intrapulmonary shunt during general anaesthesia is the development of atelectasis [20]. Atelectasis leads to intrapulmonary right to left shunts [15], which can be assessed by a decrease of the oxygenation index (PaO_2/FiO_2) [16]. In patients undergoing coronary artery bypass grafting El-Khatib and Jamaleddine [21] found significant correlation between PaO_2/FiO_2 ratio and intrapulmonary shunt. An increase in PaO_2/FiO_2 was found in patients given FiO_2 0.4 compared to patients given FiO_2 1.0 during laparoscopic cholecystectomy [22]. Staehr et al. [23] did not find difference in oxygenation index when compared FiO_2 0.3 with FiO_2 0.8 in abdominal

surgery but could not reject the possibility that 80% oxygen for a prolonged period may affect PaO_2/FiO_2 among patients with cardiovascular comorbidity.

In our study the patients underwent to thoracic surgery having more risk for atelectasis formation. We found that PaO_2/FiO_2 decreased during the operations in both H and L groups (Table 2). But if compared between the groups, the mean PaO_2/FiO_2 values were low in the group H (Figure 1). So, we can say that during the operations atelectasis were formed more intensively in the group with higher FiO_2.

Atelectasis formation as well as physiologic dead space changes are correlated with the duration of anaesthesia [24,25]. The groups in our study were comparable according to anaesthesia time (227 ± 38 min vs 224 ± 35 min p = 0.784).

A hyperoxia-induced reduction in cardiac output may contribute to an increase in $P(a\text{-}Et)CO_2$ and VDalv. The decrease in cardiac output increases $P(a\text{-}Et)CO_2$ and VDalv by causing the decrease in CO_2 elimination from alveoli and the redistribution of pulmonary blood flow. Isserles and Breen [26] reported that during constant minute ventilation and tissue VCO_2, there were reductions in $PEtCO_2$ of 7.4% and $PaCO_2$ of 4.7% which resulted in the increase in $P(a\text{-}Et)CO_2$ when the reduction in cardiac output was 10%. Anderson and colleagues [27] reported, that under sevoflurane anaesthesia cardiac output increased by 5.8% when FiO_2 was changed from 1.0 to 0.3. Harten JM and colleagues [28] reported, that cardiac output decreased by 10.6% after a change in FiO_2 from ≤0.6 to 1.0 in patients after coronary artery bypass surgery. In 2018 Smit et al. [29] studied Hemodynamic effects of acute hyperoxia. In their Systematic review and meta-analysis, the authors found, that hyperoxia (PaO_2 of 234–617 mmHg) may considerably decrease cardiac output and increase systemic vascular resistance (SVR), but effects differ between patient categories. No significant changes in cardiac output were seen in CABG patients, but SVR increased by 15.9%.

We did not measure cardiac output directly but compared the groups according to the hemodynamic data and the doses of the medication affecting on cardiac output. We did not find any significant difference between them. We also evaluated blood lactate and creatinine levels that secondarily might had been affected by the changes of cardiac output. The H and L groups were comparable according to the laboratory data (Table 4).

In our study $P(a\text{-}Et)CO_2$ gradient mean values were different between H and L groups. The patients in the H group were ventilated with FiO_2 80% and had greater $P(a\text{-}Et)CO_2$ gradient comparing with the group L where the patients received 50% of inhaled oxygen concentration (Figure 1). Taking into account that the patients in both groups were anesthetized under same condition except of FiO_2 and assuming that they had similar cardiac output, we can say that inhaled oxygen concentration had an impact on pulmonary gas exchange. We assessed $PaCO_2/PEtCO_2$ ratio as an indicator of pulmonary gas exchanger performance. As mentioned above it may be considered a "positive variable" (greater the ratio, better the gas exchange) [17]. We found that the patients had better $PaCO_2/PEtCO_2$ ratio if ventilated with lower FiO_2 (Figure 1).

Recently was published a systematic review and meta-analysis of randomized controlled trials: "Effects of high versus low inspiratory oxygen fraction on postoperative clinical outcomes in patients undergoing surgery under general anesthesia" [30]. Twenty-six trials with a total 4991 patients were studied. The authors concluded that there is a lack of evidence that the high FiO_2 compared to low FiO_2 has a deleterious impact on the mortality in adult patients undergoing non-thoracic surgery under general anesthesia. The incidence of pneumonia, respiratory failure, PPCs, ICU admissions, and length of hospital stay were comparable between the groups; while the incidence and the severity of atelectasis were increased and postoperative PaO_2 was lowered by high FiO_2. It is suggested that clinicians should not be reluctant to administer a high FiO_2 in an effort to reduce adverse events during general anesthesia. In our study we also found that high FiO_2 (0.8) worsens pulmonary gas exchange performance compared with low FiO_2 (0.5), but it doesn't have an adverse impact on the duration of postoperative mechanical ventilation and ICU length of stay (Table 4).

In 2016 two trials have attempted to demonstrate that avoidance of hyperoxia during cardiac surgery reduces ischemia-reperfusion injury and leads to improved clinical outcomes [31,32]. McGuinness et al. [31] randomized 298 elective cardiac surgery patients to either avoidance of intraoperative hyperoxia (with a PaO_2 target of 75-90 mmHg) or to usual care under hyperoxic conditions. They found no difference between groups for the primary outcome of postoperative acute kidney injury (AKI), or any of the secondary outcomes. In a similar trial, Smit et al. [32] randomized 50 elective coronary artery bypass graft (CABG) surgery patients to either a PaO_2 target of 130 to 150 mmHg on CPB (and 80-100 mmHg in the immediate postoperative period) or a target of 200 to 220 mmHg on CPB (and 130-150 mmHg postoperatively). Again, the conservative oxygen strategy did not offer any benefit with respect to the primary outcome of myocardial injury (defined by suitable CK-MB and Troponin-T thresholds). Cardiac index, systemic vascular resistance index, creatinine, lactate and F2-isoprostane levels were not different between groups.

According to our study, H and L groups were comparable according to laboratory data and hemodynamic profile as well (Table 4).

Recently, Ju et al. [4] hypothesised that a mild supra-physiologic level of oxygen tension (i.e., mild hyperoxia) would improve post- operative mortality in patients undergoing OPCABG. Their study aimed to evaluate the relationship between intraoperative PaO_2 and mortality following OPCABG. The authors concluded, that intraoperative mild hyperoxia (PaO_2 of 150–250 mmHg) was associated with a significantly lower risk of in-hospital mortality after OPCABG than normoxia/ near-normoxia (PaO_2 < 150 mmHg) and severe hyperoxia (PaO_2 > 250 mmHg).

In our study PaO_2 mean values were different at start and end points of anaesthesia. In the group H the mean PaO_2 ranged 233 – 280 mmHg and in the group L _ 161-181 mmHg (Table 2). That difference of PaO_2 level between the groups did not alter the outcomes we studied (Table 4).

Conclusion.

FiO_2 0.8 is associated with more derangements of pulmonary gas exchange compared with FiO_2 0.5 in patients undergoing

sevoflurane anaesthesia during OPCABG. FiO_2 had an impact on PaO_2/FiO_2 ratio, $P(a\text{-}Et)CO_2$ gradient and $PEtCO_2/PaCO_2$ ratio. The patients ventilated with FiO_2 0.8 had more $P(a\text{-}Et)CO_2$ gradient, less $PEtCO_2/PaCO_2$ ratio and less PaO_2/FiO_2 ratio at the end of OPCABG operations compared with the patients ventilated with FiO_2 0.5. Although FiO_2 did not have an impact on the outcomes we studied, using FiO_2 0.5 seems to be safer in patients undergoing OPCABG.

Conflict of interest.

The authors declare no conflict of interest.

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