

GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 9 (366) Сентябрь 2025

ТБИЛИСИ - NEW YORK



ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии
საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press.
Published since 1994. Distributed in NIS, EU and USA.

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 ВИНТИ 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 ВИНТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებში.

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. Корректур авторам не высылаются, 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 computer-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 საყურადღებო!

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, შემავსებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრაფიის ფოტოსურათები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შედეგების 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 ფხიხლებში 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.

Takuma Hayashi, Kaoru Abiko, Ikuro Konishi. CHARACTERISTIC OF MYELOID SARCOMA BY CANCER GENOME PROFILING AND ALGORITHM OF POTENTIAL BIOMARKERS FOR UTERINE MESENCHYMAL TUMOR.....	6-13
Feruza Abdullayeva, Kuralbay Kurakbayev, Madamin Karataev. MODERN STRATEGIES IN OUTPATIENT STROKE CARE: A SYSTEMATIC REVIEW OF METHODS, TECHNOLOGIES, AND PROSPECTS.....	14-24
Shota Janjgava, Elene Giorgadze, Revazi Jamburia, Ana Davitashvili, Ketevan Asatiani. RECOMMENDATIONS FOR THE MANAGEMENT OF DIABETIC FOOT.....	25-32
Isoyan A.S, Danielyan M.H, Antonyan I.V, Azizyan N.H, Mkrtchyan A.A, Nebogova K.A, Karapetyan K.V. CHANGES IN THE MORPHOLOGICAL AND FUNCTIONAL STATE OF HYPOTHALAMUS NUCLEI NEURONS IN LONG-TERM CRUSHING SYNDROME.....	33-40
Saduakassova Korlan Zarlykovna, Kassenova Gulzhan Toktaubekovna, Issayeva Raushan Binomovna. EPIDEMIOLOGY AND DIAGNOSTIC CHALLENGES OF AUTISM SPECTRUM DISORDERS IN CHILDREN IN THE REPUBLIC OF KAZAKHSTAN.....	41-46
Nurbol Tursynbaev, Samat Zharmenov, Altyn Dossanova. IMMUNISATION OF CHILDREN IN KAZAKHSTAN: ASSESSMENT OF COVERAGE AND BARRIERS TO VACCINATION REFUSALS IN THE CONTEXT OF SOCIAL NETWORKS AND PARENTAL BELIEFS.....	47-56
Tariel V. Ghochikyan, Melanya A. Samvelyan, Armen S. Galstyan, Karine S. Avetisyan. BIOLOGICAL STUDIES OF THIAZOLES OF NEW STRUCTURE.....	57-63
Yahya Qasem Mohammed Taher, Safeyya Adeeb Ibrahim, Duaa Mohammed Ahmed. BENIGN FASCICULATION SYNDROME AMONG HEALTH CARE WORKERS, A SINGLE CENTER STUDY.....	64-68
Marine A. Parsadanyan, Hrant M. Avanesyan, Arsen B. Lokyan, Sahak V. Hovhannisyan, Mariam A. Shahinyan, Marieta S. Mikaelyan, Gaspar H. Kocharyan, Ara P. Antonyan, Poghos O. Vardevanyan. INTERACTION OF DOPAMINE WITH DNA, DEPENDING ON THE IONIC STRENGTH OF THE SOLUTION: POTENTIAL APPLICATION IN SENSOR TECHNOLOGY.....	69-75
Ahmed Alaa Al-Temimi, Raja Ezman Raja Sharif, Mohd Shahezwan Abd Wahab, Hanis Hanum Zulkifly. GUIDELINE-DIRECTED MEDICAL THERAPY (GDMT) FOR HEART FAILURE MANAGEMENT: ADDRESSING APPLICATIONS, BARRIERS AND OPTIMIZING IMPLEMENTATION.....	76-83
Yerbolat Iztleuov, Marat Iztleuov, Anar Tulyayeva, Gulmira Iztleuova, Elyanora Kydyrbayeva. THE USE OF HERBAL MEDICINES IN PREVENTING CANCER MUTATIONS IN ANIMAL MODELS EXPOSED TO TOXICANTS: A SYSTEMATIC REVIEW.....	84-92
Mazyad M Alenezi, Faisal A. Al-Harbi, Rana S. Alqurini, Abdulrahman M. Aloufi, Sulaiman M. AlMushawwah, Mohammed S. Alkhaldi, Reman H. Alsaqrh, Abdullah Yahya Asiri, Manar O. Alharbi, Sultan Alanazy. HOW PRIMARY HEALTH CARE PHYSICIANS IN SAUDI ARABIA HANDLE SUDDEN SENSORINEURAL HEARING LOSS: A CROSS-SECTIONAL STUDY.....	93-100
Hussein A Saheb, Hussam H Sahib, Ahmed M sultan, Luma hassnaui. THE INCIDENCE OF URINARY TRACT INFECTION AMONG PATIENTS TREATED WITH VARIABLE DOSES OF DAPAGLIFLOZIN: A COMPARATIVE STUDY.....	101-105
Ilia Nakashidze, Ahishtan Febrian Nishanthan, Shota Nakashidze, Aleena Parveen Shaikh, Nameera Parveen Shaikh, Naman Chauhan, Salome Zoidze, Sarfraz Ahmad, Irina Nakashidze. PRECISION MEDICINE AND ANAESTHESIA: CURRENT CLINICAL AND GENOMICS APPROACHES.....	106-116
Gasparyan Diana V, Shishkova Valeria E, Gevorgyan Sergey A, Podorovskaya Alexandra I, Kudryashova Arina A, Parfilova Elizaveta A, Poltoratskaya Karina D, Djurabaeva Gulnozahon S, Patsukova Anastasia V, Bolban Svetlana E. PRIMARY HYPERPARATHYROIDISM: DIAGNOSTIC DIFFICULTIES AND RARE MANIFESTATION IN THE FORM OF HYPERCALCAEMIC CRISIS.....	117-119
Uday Mahajan, Muhammad Yousaf, Fahad Jalil, Asif Afridi, Meraj Akhtar, Haroon Yousaf, Amna Hilal, Adnan Asif, Muzammil Ahmed Khan, Anurag Dureja, Mohammed Jaffer Ali, Madeeha Hussaini. REVIEW OF INTRA-OPERATIVE TECHNIQUES TO ASSESS REDUCTION QUALITY IN TIBIAL PLATEAU FRACTURES.....	120-123
Sara Abdelmehmoud Omer, Abdelkarim Abobakr Abdrabo, Afif Abdelmehmoud Omar, Einas A Osman. DIAGNOSTIC AND PROGNOSTIC VALUE OF ANTI-CYCLIC CITRULLINATED PEPTIDE AND RHEUMATOID FACTOR IN RHEUMATOID ARTHRITIS PATIENTS.....	124-128
Alan Adnan Saber. A DESCRIPTIVE STUDY ON THE TRENDS OF CAUSATIVE BACTERIA AND ANTIMICROBIAL RESISTANCE PROFILES IN PATIENTS WHO DEVELOPED SEPSIS FOLLOWING GASTRIC SLEEVE RESECTION.....	129-134

Kuralay Amrenova, Askar Serikbayev, Altay Dyussupov, Alua Sharapiyeva, Altynay Dosbayeva, Ainur Krykpayeva, Ynkar Kairkhanova, Nazym Kudaibergenova, Zhanar Zhumanbayeva. HEALTH-RELATED QUALITY OF LIFE OF POST-COVID-19 PATIENTS IN KAZAKHSTAN.....	135-140
Anar Tulyayeva, Iztleuov Yerbolat, Dinara Zholmukhamedova, Nauryzbay Imanbayev, Maya Alibekova. CORRELATION OF HER2 STATUS WITH LYMPH NODE METASTASIS IN KAZAKH PATIENTS WITH GASTRIC.....	141-147
Ahmad MT. Kurukchi, Afya SD. Al-Radha, Athraa A. Mahmood. RADIOGRAPHIC EVALUATION OF THE IMPACT OF PRF MEMBRANE LAYERING ON PERI-IMPLANT TISSUE: RANDOMIZED CONTROLLED CLINICAL TRIAL.....	148-154
Berdia Beridze, George Gogniashvili. LINGUISTIC VALIDATION, PSYCHOMETRIC EVALUATION AND CROSS- CULTURAL ADAPTATION OF THE GEORGIAN SINO- NASAL OUTCOME TEST.....	155-159
Sahib Memon, Mustafa Al-Yassen, Uday Mahajan, Sirtaaj Mattoo, Karim Hussien. OPERATIVE VERSUS NONOPERATIVE MANAGEMENT OF SALTER-HARRIS TYPE II DISTAL RADIUS FRACTURES IN CHILDREN: A RETROSPECTIVE COHORT STUDY.....	160-163
Z.E. Alshimbayeva, R.Kh. Begaydarova, N.M. Khodzhaeva, G. K. Alshynbekova, B.K. Koichubekov, Zolotaryova O.A. IMMUNOLOGICAL CRITERIA FOR PREDICTING SEVERE AND COMPLICATED FORMS OF VARICELLA ZOSTER IN CHILDREN.....	164-169
Anastasiia Shumarova. COPING STRATEGIES IN CONDITIONS OF CONTINUOUS TRAUMATIC STRESS: COMPARATIVE ANALYSIS WITHIN THE CONTEXT OF ARMED CONFLICT.....	170-177
Noha O Mohamed, Rayan Yousef, Abobuker Elgak, Mohammed Mohammed, Sara Mohammed, Amna Mustafa, Tayseer Ahmed, Mutwakil Mubarak. PARADOXICAL ELEVATION OF PLATELET INDICES IN SUDANESE PATIENTS WITH CHRONIC HEPATITIS B: A CROSS- SECTIONAL ANALYSIS.....	178-183
Lyazzat Alibekova, Dinara Ospanova, Arailym Muratkhan, Bibinur Abdimuratova, Makhigul Maxudova. SELF-ASSESSMENT ON LEADERSHIP SKILLS OF NURSING SERVICE MANAGERS IN KAZAKHSTAN.....	184-188
Ze-Quan Liu, Wei-Wei Chang, Long Hua, Li-Jun Zhu, Li-Ying Wen, Jia-Jing Zhao, Yi-Chen Li, Ying-Shui Yao, Yue-Long Jin. THE RELATIONSHIP BETWEEN NEGATIVE EMOTIONS AMONG BOARDING SCHOOL STUDENTS IN CERTAIN REGIONS OF ANHUI PROVINCE AND FAMILY ENVIRONMENT AND EDUCATIONAL METHODS.....	189-195
Zozulya Aleksei V, Teslevich Vladislav S, Abkhazava Peride, Ramazanov Islam A, Tokhtarova Snezhana V, Streltsova Olga V, Kalsynov Gamzat M, Chernogoloviy Artem S, Antun Djemi F, Gamzaeva Saida T. COMPARATIVE ASSESSMENT OF THE EFFECT OF SILYMARIN, FENOFIBRATE, BETAINE AND ADEMETIONINE ON THE DEVELOPMENT OF STEATOHEPATITIS IN WISTAR RATS.....	196-200
Maira Zh. Espenbetova, Alexandr Zubkov, Ainur S. Krykpayeva, Aida M. Bidakhmetova. CYTOLOGICAL EXAMINATION OF THYROID NEOPLASMS IN INDIGENOUS RESIDENTS LIVING IN THE FORMER SEMIPALATINSK NUCLEAR TEST SITE AREA.....	201-207

PRECISION MEDICINE AND ANAESTHESIA: CURRENT CLINICAL AND GENOMICS APPROACHES

Ilia Nakashidze^{1*}, Ahishtan Febrian Nishanthan¹, Shota Nakashidze², Aleena Parveen Shaikh¹, Nameera Parveen Shaikh³, Naman Chauhan¹, Salome Zoidze¹, Sarfraz Ahmad⁴, Irina Nakashidze^{5*}.

¹Department of Critical Medicine, Faculty of Natural Sciences and Health Care, Batumi Shota Rustaveli State University, Batumi, Georgia.

²Wolfson Medical Center, Holon, Israel.

³School of Occupational and Public Health, Toronto Metropolitan University, Toronto, ON, Canada.

⁴AdventHealth Cancer Institute, Orlando, FL, USA.

⁵Faculty of Natural Sciences and Health Care, Batumi Shota Rustaveli State University, Batumi, Georgia.

Abstract.

The field of anaesthesia, or anesthesiology, has undergone several advancements in recent years, becoming more precise and personalized to patients' needs, and more viable in clinical settings. As a result, anesthesiology has become more viable in clinical settings, tailored to patients' needs. Furthermore, it is not only the intraoperative care during surgery that requires attention, but also the pre-operative and post-operative care, as any coexisting conditions can obstruct proper pain management and recovery, and also to focus on any preexisting comorbidities to provide a more personalised anaesthesia care. And when it comes to a personalised anaesthesia plan, the patient's genomic data plays a crucial role, as it can enhance not only the effectiveness of the anaesthetics used but also the safety and reliability of total anaesthesia care. Therefore, pharmacogenomics is a critical factor in the evolution of anesthesiology and, furthermore, also plays a pivotal role in precision medicine. In this review, we revise Current Clinical and genomics approaches regarding anaesthesia. Taken all together, the field of anaesthesia is increasingly dependent on precision and personalised approaches, thereby significantly improving patient safety. A greater focus on personalised approaches can be achieved by fully incorporating pharmacogenomics; it is precisely based on the patient's genetic characteristics that individualized treatment plans can be developed. Identifying specific genetic markers that affect drug metabolism and efficacy will enable clinicians to enhance the effectiveness and safety of anaesthetic care. Accordingly, the transition from a generic approach to a more tailored strategy significantly reduces the risk of adverse drug reactions, while also contributing to and focusing on better therapeutic outcomes. Overall, it contributes to patient recovery and a better prognosis. Pharmacogenomics, nanotechnology, three-dimensional printing technology, and AI hold potential to transform precision anaesthesia, enhancing perioperative care by providing patient-centered drug delivery systems, customized surgical tools, and improved therapeutic outcomes personalised to patients' needs.

Key words. Precision medicine, anaesthesia, genomics approach.

Introduction.

Anesthesia, a medical intervention, provides a state of controlled loss of pain reception or sensation for medical procedures,

includes three main categories: General anesthesia, Regional and Local anesthesia [1,2] Anesthesiology is considered a complex medical specialty [2-5] The field of anesthesia or anesthesiology in recent years has undergone several advancements to become more precise and personalized to patients' needs, to be more viable in clinical settings. Advances were not only focused on precision and personalisation but also on providing the best patient safety, because during the initial development of anesthesiology, the practice faced several setbacks related to patient safety, and so, along with the growth in pre-operative preparation and antibacterial techniques, patient safety in anaesthesia also developed [6]. Furthermore, it is not only the intraoperative care during surgery that requires attention, but also the pre-operative and post-operative care, as any coexisting conditions can obstruct proper pain management and recovery, and also to focus on any preexisting comorbidities to provide a more personalised anaesthesia care [7]. And when it comes to a personalised anaesthesia plan, the patient's genomic data plays a crucial role, as it can enhance not only the effectiveness of the anaesthetics used but also the safety and reliability of total anaesthesia care. Additionally, when it comes to patient responses to anesthesia, genetic factors can outweigh several factors such as age, mass index, underlying diseases, and gender. However, when it comes to geriatric patients, age is a factor to be considered, as renal clearance can pose a significant threat to the drug clearance rate and impact the effectiveness of the drugs used [8,9].

Precision medicine has gained increasing attention across many medical fields, with the goal of adapting treatment to the genetic and physiological profile of each patient [10,11]. In anesthesiology, this approach could allow more accurate drug selection, safer dosing, and better prediction of perioperative outcomes [12]. However, despite this promise, current practice in anesthesia still relies heavily on population-based guidelines and standardized protocols, creating a gap between the potential of precision medicine and its application in routine care [13,14].

Currently, anesthesiology remains largely protocol-driven, with clinicians utilizing established drug regimens and monitoring systems that apply broadly to most patients. While this has ensured safety and efficiency, it does not always account for individual variability in drug metabolism, genetic background, or comorbid conditions [15]. Some progress has been made through pharmacogenomics research, such as the role

of CYP2D6 in opioid metabolism and variability in response to anesthetic agents [16].

Several barriers limit the widespread use of precision medicine in anesthesiology. From a scientific perspective, there are still few validated biomarkers that can reliably guide anesthetic choice or dosing. Genetic influences on drug metabolism are complex and often vary across populations, and the interaction between multiple genes and clinical factors is not fully understood [15-18]. Clinically, the integration of precision tools into the perioperative workflow is difficult. Patient responses to anesthetic agents remain highly variable, and there is limited availability of real-time decision support that can help anesthesiologists adapt care on the spot [18-20]. On a practical level, precision medicine approaches are hindered by the high cost of genetic testing and the lack of infrastructure to integrate data into electronic health records and bioinformatics systems [21]. Ethical and privacy concerns related to genetic data further complicate implementation. In addition, many clinicians have not yet received training in the interpretation and application of precision medicine findings, creating knowledge gaps in practice [22,23]. Finally, there is a significant evidence gap. Large, diverse clinical trials are still needed to demonstrate that precision-based strategies provide superior outcomes compared to current standard protocols. Without strong clinical evidence, widespread adoption remains unlikely [24].

Looking ahead, several opportunities could support the growth of precision medicine in anesthesiology. One major area is the expansion of pharmacogenomic testing, including the development of rapid perioperative genetic screening that can provide results in time to guide anesthetic choice and dosing [18-26]. Artificial intelligence and machine learning also offer potential by integrating genetic, physiological, and intraoperative data into real-time decision-making tools. Improved perioperative risk prediction is another important direction, particularly for

vulnerable groups such as elderly patients, those with multiple comorbidities, or individuals undergoing complex cancer surgeries [27,28]. Finally, the development of cost-effective, point-of-care precision tools will be essential for adoption in everyday practice. Affordable and accessible technologies could help overcome financial and logistical barriers, allowing precision medicine approaches to be applied more widely across different healthcare settings [29,30].

Therefore, pharmacogenomics is a critical factor in the evolution of anesthesiology and, furthermore, also plays a pivotal role in precision medicine. It helps clinicians to tailor personalised treatment plans for the patients by identifying the specific genetic markers that affect drug metabolism, efficacy and patient safety. This approach not only minimises the risk of complications that can arise from adverse drug reactions but also improves therapeutic outcomes by selecting the most effective drug at the optimal dose. And so, pharmacogenomics serves as a cornerstone of precision medicine, transitioning from a one-size-fits-all model to a more individualised plan that benefits the patients and prevents adverse complications [31].

This review paper explores and analyzes the current clinical and technological approaches in anesthesia, emphasizing the importance of precision medicine in enhancing anesthetic care.

Precision Medicine and Genetic factors in anesthesia care.

Precision medicine personalizes healthcare by combining a patient's genetic variants and medical history. It has demonstrated potential application in addressing various health challenges; its primary goal is to improve treatment effectiveness, patient outcomes, reduce complications and tailor healthcare. Precision medicine is also capable of understanding in-depth variations in the patient's genetic factors, paving the way for more personalised care [32,33]. It can also measure risk assessment and prevention by identifying individuals with genetic predispositions that pose a high risk of certain conditions. This helps develop proactive measures, such as lifestyle changes and early screening, which contribute to preoperative management in anaesthesia care [34]. On the other hand, even though traditional anaesthetic protocols work for most patients, they are incapable of accounting for how individuals respond to drugs or to treatment. These variations can lead to unexpected complications which can affect treatment outcomes. This leads to the integration of pharmacogenomics in precision medicine to provide personalized anesthesia care [35].

Pharmacogenomics, the field that comprehends drug efficacy and toxicity at the genetic level based on genetic variations affecting pharmacokinetics and pharmacodynamics, can guide the development of optimal therapeutic strategies [36]. This is particularly relevant in understanding how a person responds to drugs, as it depends on the drug-metabolising enzymes and their genetic variations, which are responsible for activating and breaking down drugs. Drug-metabolizing enzymes play a role in converting prodrugs to their usable-active form in the body, however any genetic mutation or deficiency in these enzymes can affect this conversion leading to drug ineffectiveness and those drugs that are not capable of breaking down can lead to accumulation and then result in drug-toxicity and its adverse side effects, which is why genetic variants are considered a crucial information in anesthesia care [37]. The significance of pharmacogenomics in anaesthesia care can be further understood by considering the example of cytochrome P450 enzymes. Cytochrome P450, a family of enzymes belonging to the group B cytochromes, is responsible for the metabolism of drugs, steroids and fatty acids. This group of enzymes includes NADPH cytochrome C reductase (flavoprotein), phosphatidylcholine (phospholipids) and P450 (haemoglobin). Cytochrome P450, although found in cells of lungs, brain, kidneys, gastrointestinal tract, placental tissue and skin, is present in higher concentrations in the liver [35]. These enzymes are also capable of protecting against foreign compounds and additionally can convert drugs to more reactive compounds [38]. The CYP family that is considered to be related to a broad range of substrates and is found to be in high concentrations is the Cytochrome P4503A (CYP3A), which includes CYP3A4, CYP3A5, CYP3A7 and CYP3A43 [39]. Understanding CYP3A family is considered necessary in places where it is required to correlate genetic factors and ethnic differences, that is, to be more specific, CYP3A5 which accounts for over half of total hepatic CYP3A, under which the CYP3A5*1 allele is most commonly found among African population is linked to higher CYP3A5 expression, on the other hand it is found to have minimal impact on drug metabolism in

Caucasian population. Therefore, ethnic differences in CYP3A5 expression play a role in the variations of CYP3A-mediated metabolism. Additionally, changes in CYP450 enzymes such as CYP2D6, CYP3A4 and CYP2C9 can influence anaesthetic metabolism. For example, patients with improper CYP2D6 metabolizers can have prolonged drug effects or reduced pain relief with agents like codeine, while patients who have rapid metabolizers can suffer from drug toxicity due to excess active metabolites [40]. Therefore, this highlights the significance of understanding genetic variants to enhance anaesthesia outcomes and prevent complications [41].

Thus, it is suggested that, by considering individual genetic variants in conjunction with patients' medical histories, treatment effectiveness and patient outcomes can be enhanced, thereby supporting minimising complications. Specifically, the limitations of traditional anaesthetic protocols are not focusing on examining the individual variations regarding drug response, which potentially leads to adverse effects.

Importance of understanding anaesthesia in the perioperative period during cancer.

To further highlight the importance of personalised anaesthesia care, it is helpful to consider its role in cancer. Even though there have been advances in early diagnosis, surgery and cancer management, postoperative cancer recurrence and metastasis still remain a major concern. This tumour recurrence and development are closely associated with the perioperative period, which also encircles anaesthesia administration and its management [42]. For instance, some anaesthetics such as propofol, lidocaine, and ropivacaine have demonstrated anti-tumour effects by preserving immune functions and inhibiting tumour growth; on the other hand, volatile anaesthetics such as isoflurane, sevoflurane, and desflurane may contribute to tumour progression and metastasis [43]. Therefore, perioperative anaesthesia care that supports immune functions is considered essential, and selecting anaesthetic agents based on their oncological impact and the patient's genetic profile can optimise surgical outcomes and prevent adverse side effects such as the risk of recurrence [44,45].

To optimise anaesthesia and reduce complications, it is crucial to integrate pharmacogenomics approaches to maximise drug efficacy and reduce toxicity. Genetic variations in some genes can lead to significant differences in drug metabolism.

Importance of understanding anaesthesia's current approaches in complex disease' management.

Precision medicine is suggested to ensure that medical interventions are tailored to an individual's unique genetic, environmental, and lifestyle characteristics. At the intersection of genetics and anesthesiology. It applies these principles by sculpting anesthetic is the field of personalised anaesthesia, which is frankly still evolving every day. It applies these principles by sculpting anaesthetic regimens around a patient's specific genetic predispositions, comorbidities, and physiological parameters. The foundational pillars of this approach include pharmacogenomics, advanced biomarker analysis, and the role of artificial intelligence. Patients with cardiovascular diseases are specifically susceptible to adverse events. The traditional model of medicine, often characterised

by a "one-size-fits-all" approach, is rapidly giving way to the more nuanced framework of precision medicine. Today, our medical community is well aware of the concept of personalised anaesthesia, for example, as a perioperative measure that potentially directly affects the outcomes of procedures. The ultimate goal may be to move beyond conventional protocols to mitigate perioperative complications, refine pain management, enhance recovery after surgery (ERAS) protocols, and improve patient safety and satisfaction. Hippocrates believed that it was essential to understand the person with the disease to effectively treat them; thus, this is not entirely a new concept in healthcare. In fact, anesthesiologists are likely the first physicians to seriously undertake personalized and precision medicine, as even the oldest records show them using unique amounts, titrating the dose based on direct, real-time observation of the patient's clinical effects and specific clinical features. Modern personalised anaesthesia is not a radical departure, but a logical evolution, empowered by powerful new technologies and the ability to interpret vast quantities of acute care data [46]. Even though the risk factors are identified and improvements have been made in treatments for prevention, PONV (postoperative nausea and vomiting) rates are still as high as 80% in the circumstances of high risk [47]. The importance of personalised anaesthesia in patients with CVD is of an imperative nature as they are more susceptible to the risks perioperatively, such as hemodynamic instability, arrhythmias, and ischemic events. [48]. The optimisation of perioperative approaches is crucial for achieving positive outcomes in procedures for high-risk groups [49]. Specific genetic variations have been shown to have a significant impact on anesthesia outcomes. Malignant hyperthermia (MH), a rare but life-threatening hypermetabolic response to certain anesthetic drugs, is a genetically determined autosomal dominant disorder [50]. The majority of cases are linked to mutations in the RYR1 gene, which provides instructions for a protein involved in the regulation of calcium ions in skeletal muscle cells [51]; These genetic variants cause the RYR1 channel to open more easily and close more slowly in response to halogenated anesthetics, such as isoflurane and sevoflurane, and the neuromuscular blocker suxamethonium. The resulting flood of calcium ions leads to muscle rigidity, heat generation, and acidosis, demonstrating a direct, heritable link between genotype and a dangerous adverse reaction. The metabolism of opioids like codeine and tramadol is dependent on the CYP2D6 enzyme. Individuals classified as poor metabolizers of this enzyme may experience little to no analgesic effect from these prodrugs, as they are unable to effectively convert them to their active form. Conversely, ultrarapid metabolizers may produce abnormally high levels of morphine from standard doses of codeine, leading to a rapid onset of side effects. The OPRM1-A118G polymorphism has been linked to a reduced risk of postoperative vomiting, though not other side effects like nausea or pruritus. In the context of the public health crisis surrounding opioid addiction, the determination of genetic profiles susceptible to respiratory depression is a critical area of ongoing research [52,53]. Similarly, the metabolism of the beta-blocker metoprolol, commonly used in patients with CVD, is mediated by the CYP2D6 enzyme. A study found that poor metabolizers of CYP2D6 experienced an increased risk of

bradycardia and had a significantly lower average heart rate compared to normal metabolizers. These findings underscore the need for personalised dosing to minimise adverse effects, further solidifying the case for pharmacogenomic testing [54]. Another important factor for patients with heart failure is the measurement of prognostic biomarkers like Natriuretic Peptides, soluble ST2 receptor, and galectin-3, which guide treatment strategies, leading to reduced mortality and improved quality of life. These protein-based biomarkers are easily accessible in circulation and provide valuable, tissue-specific information that informs therapeutic guidance [55]. To not discuss about the future and the fastest currently evolving part of this topic would be injustice, to AI and machine learning which are using the vast and often abundant amount of perioperative data being collected by EMG and NMT sensors to help in providing more precise details that may enable anesthesiologists to make better choices during procedures such as finding the optimal titration of anesthetic agents required for the patient. A prime example is the Hypotension Prediction Index (HPI), a validated machine learning algorithm that predicts hypotensive events in surgical patients. By analysing high-fidelity arterial pressure waveforms, the HPI can provide an early warning up to 15 minutes in advance, allowing clinicians to act proactively. Studies have shown that the use of HPI software, when combined with a treatment protocol, can achieve a statistically significant reduction in both the incidence and duration of intraoperative hypotension. While these predictive models demonstrate high accuracy, it is important to note their limitations; some models may rely on a single data source or may not be able to identify the specific root cause of an event, reinforcing the role of these tools as an augmentation to, rather than a replacement for, human clinical judgment [56].

General anesthesia is superior to conscious sedation in the successful reperfusion rate for acute ischemic stroke patients undergoing endovascular therapy, but is associated with higher risks of hypotension and pneumonia [33]. It is suggested that machine learning shows promise in stroke medicine, enabling precise diagnosis, tailored treatment selection, and improved prognosis, but challenges must be addressed for widespread adoption and impact [57]. Genetic variations in electroencephalogram phenotypes can influence the depth of general anaesthesia during surgery, potentially impacting the accuracy of bispectral monitoring. Six SNPs in five genes were associated with EEG spindle amplitude during anaesthesia [58]. Some specific SNPs, namely SCN9A, SCN10A, and SCN11A, play a significant role in postoperative inadequate analgesia following single-port VATS [59].

In conclusion, the evolving field of personalised anaesthesia highlights the importance of tailoring medical interventions to individual patient characteristics, including genetic, environmental, and lifestyle factors. This approach not only supports patient safety and satisfaction but also minimises perioperative complications, especially in high-risk populations such as those with cardiovascular diseases and stroke.

Nanotechnology and Three-dimensional Printing technology in precision anaesthesia.

The advanced technological approaches have transformed the field of anesthesia, leading to more precise and personalized

care. The application of nanotechnology is closely related to the drug delivery system in the body. Nanotechnology, specifically nanomedicine, has been a pivotal technological advancement in recent years due to its ability to provide a targeted drug delivery system, which in turn can lead to improved therapeutic efficacy and minimise systemic side effects, highlighting its significance in precision medicine and anaesthesia [60]. It involves unique encapsulated nanoparticles and bio-interactive surface modifications which is a part of the drug-delivery system [61]. It is especially advantageous when it comes to the slow drug release effect of the medications used, which also includes anaesthetics, as certain anaesthetics in patients with a genetic predisposition can cause fast metabolism and a higher drug clearance rate, and so this property of nanoparticles becomes advantageous in such cases [62]. Additionally, nanomedicine can also assist in increasing drug permeability and prolonging the anaesthetic action, specifically a hybrid nanofilm with lidocaine and prilocaine can demonstrate this property [63]. This property is considered a significant benefit for patients who require extended pain management or those experiencing chronic pain conditions. Therefore, an anesthesiologist can utilise nanotechnology in routine clinical anaesthesia and pain management to improve perioperative care and reduce perioperative-related complications [64,65].

Three-dimensional printing technology is one of the most recent technological advancements which has been found in a broad range of areas of both medical science and industrial fields. It is a type of manufacturing technology that involves easily accessible and modifiable digital structuring which utilizes bondable materials like plastic, polymers and metals for manufacturing [66]. Similar to how three-dimensional imaging helps clinicians to visualize the complications in patients, three-dimensional printing assists clinicians to attain a real tactile-abled feedback model made with specific modifications from the patient's pathology [67]. This can be done by creating realistic anatomical structures that can act as functional simulators. This not only provides clinicians with the opportunity to interact freely with the models to understand the pathology, but also is considered a potent training prospect for anesthesiologists, as 3D models are cost-effective, modifiable digital renders that can be rapidly manufactured [68].

Additionally, it can also be used to print anesthesia equipment as they are both convenient and economically viable, for instance low-cost and sustainable thermal laryngoscopes have been developed with this technology [69]. Therefore taking into account the speed, cost effectiveness, sustainability of 3D printing technology it has shown to be useful in the field of precision and personalized anesthesia in providing clinicians with both insights into modifiable and individualized models based on the patient's complication for the clinical understanding and utilizing the technology further for the development of sustainable tools puts three-dimensional technology as one of the essential critical and growing technologies in precision medicine.

Thus, advances in nanotechnology and 3D printing significantly enhance anesthesia care, allowing for targeted and personalized, treatment management in clinical settings.

AI Role in Anesthesia.

According to the literature, integrating artificial intelligence (AI) genomic tools can significantly improve monitoring in anesthesiology, particularly by leveraging AI's formidable data processing/self-learning capabilities. Additionally, by statistically analysing serial data streams from anaesthesia machines and monitors, it is suggested that AI can integrate with technologies such as electroencephalography (EEG) and near-infrared spectroscopy (NIRS), accordingly providing real-time feedback to optimise patient care [8].

AI/machine learning is increasingly integrated into anaesthetic practice, aiding in the interpretation of complex genetic/genomic data and supporting advanced decision-making. AI-driven tools can synthesise genomic, clinical, and monitoring data to recommend personalised anaesthetic protocols/streamline procedures and finally significantly reduce risks. The use of big data and bioinformatics is also facilitating the identification of new genetic determinants and biomarkers relevant to anaesthesia [8,70].

A study (based on the 22 studies published between February 2019 and September 2023) suggests that the transformative impact of AI-driven models on perioperative medicine, focusing on three main domains: prediction of surgical case durations, optimisation of post-anaesthesia care unit (PACU) resource allocation, and detection of surgical case cancellations. Additionally, ML algorithms significantly enhance the precision of prognoses related to surgical durations and the risk of surgical case cancellations. These improvements have led to enhanced efficiency/cost-effectiveness/and safety in surgical procedures. For instance, XGBoost consistently outperformed other algorithms in predictive tasks, and surgeon-specific models were found to be more accurate than service-specific ones. The implementation of these models has resulted in reduced patient wait times, optimized scheduling, and better resource utilisation without negatively impacting operational efficiency or patient outcomes. Predictive models for PACU length of stay have enabled more effective case sequencing and the need for after-hours staffing. At the same time, ML-based identification of high-risk surgical cancellations has improved resource allocation and cost management. Despite these promising results, several significant challenges (related to data access, privacy concerns, validation, safety, ethical implications, etc.) are faced in the widespread adoption of AI in perioperative medicine. Importance of interdisciplinary collaboration, robustly enhancing understanding, and development of user-friendly tools to facilitate the practical implementation of AI models in healthcare settings. It suggests that Artificial intelligence in operating room management improves prediction accuracy and resource utilization, but data access and privacy concerns remain [71,72].

Taken all together, Nanotechnology/genomics and 3D printing can advance precision medicine in anesthesiology by providing personalised protocols, thereby enhancing decision-making / precision medicine [72]. The integration of specific factors, genetic makeup, biomarkers, pharmacogenomics approaches, including clinicopathological characteristics, AI artificial intelligence, will significantly contribute to personalized

anesthesia based on the patient's genetic makeup. In the case of using traditional anaesthetic protocols, individual prediction of drug reactions is not possible, and therefore, side effects are minimised. Notably, the role of pharmacogenomics involves identifying genetic polymorphisms that affect drug metabolism/sensitivity, thereby reducing the risk of complications. Despite the above, the implementation of personalised anaesthesia faces numerous challenges, including the high cost/limited availability of pharmacogenomic testing, and the lack of standardised guidelines in the case of genetic tests. However, it is undeniable that anaesthetic agents, aspects of their metabolism, treatment efficacy, and safety directly depend on drug selection and correct dosing; this approach reduces possible adverse reactions and improves therapeutic approaches. Thus, the need for the use of biomarkers is evident from the point of view of predicting/monitoring perioperative and postoperative risks.

Integrating AI and genomics in anesthesiology can improve personalized patient care and optimize existing opportunities. Notably, managing challenges related to data privacy and standardization will be critical for realizing the full potential of these advancements.

The genetic information's effect on the therapeutic decisions.

The integration of genetic information into clinical practice is no longer a theoretical concept from older times but a clinical necessity, as it offers opportunities to enhance therapeutic efficacy and minimize adverse events.

the management of Malignant Hyperthermia (MH) susceptibility, the optimization of opioid pain management, and the proactive mitigation of postoperative complications. Classical findings demonstrate that genetic variants in genes such as RYR1 and CACNA1S are not only predictive of a potentially fatal MH crisis but also help find a broader, multi-system phenotype that can guide long-term care and therapeutic applications for conditions like bleeding abnormalities, which commonly affect a significant part of our population today. In the realm of pain management, the pharmacogenomic analysis of drug-metabolizing enzymes like CYP2D6 and receptor genes like OPRM1 enables the clinicians to pre-emptively identify the patients which may be at high risk for inadequate analgesia or severe toxicity, by using a genotype-guided approach to drug and dose selection by pointing and predicting exactly how a person with a specific genotype would respond to the therapy and dosage. As far as postoperative outcomes go, Venous thromboembolism and surgical site infections are significant concerns that have been countered for a long time using classical knowledge but recently, a sophisticated understanding of genetic predispositions is emerging which not only includes using single gene variants but also polygenic risk scores and this may help the clinicians in making imperative decisions regarding therapies that directly influence the prognosis of the surgeries performed.

Fundamentally, in MH, the underlying pathophysiology involves a defect in the regulation of skeletal muscle calcium. The genetic basis of this disorder is predominantly linked to mutations in two genes: RYR1 and CACNA1S [73]. The RYR1 encodes the ryanodine receptor type 1 (RyR1), a critical calcium channel in the sarcoplasmic reticulum that controls

muscle contraction, and half of the individuals susceptible to MH carry dominant, gain-of-function mutations in RYR1. A smaller proportion of MHS cases are associated with variants in the CACNA1S gene, which encodes the α_1 s subunit of the dihydropyridine receptor (DHPR). The European Malignant Hyperthermia Group (EMHG) has verified two CACNA1S variants as being associated with MHS [74]. The Clinical Pharmacogenetics Implementation Consortium (CPIC) has established strong evidence-based recommendations for MHS-related gene-drug pairs [75]. For patients who have inherited a known MH-causative variant, the primary therapeutic decision is to avoid all the triggering anesthetic agents. Specific agents to be avoided include halogenated volatile anesthetics such as enflurane, desflurane, and isoflurane, as well as the neuromuscular blocker succinylcholine. In their place, clinicians are advised to use alternative anesthetic medications that are not known to trigger MH. These include propofol, benzodiazepines, opioids, nitrous oxide, and non-depolarizing neuromuscular blockers like rocuronium and vecuronium. This genetic-guided approach fundamentally alters the standard perioperative management plan for these patients, ensuring their safety and avoiding a life-threatening event. Recent research has revealed that the mutations are associated with broader pleiotropic effects, going beyond the anesthetic agents perspective; for instance, the mounting evidence suggested that susceptible individuals may also develop MH-like symptoms in response to exercise or exposure to hot environments, completely independent of anesthetic drugs [76].

Since the pharmacokinetic and pharmacodynamic properties of the drugs administered are largely determined by CYP450 and mu opioid receptor (MOR), respectively, genetic variations in the genes encoding these proteins are key determinants of a patient's response to opioid therapy [77,78]. The CYP2D6 enzyme, encoded by the CYP2D6 gene, is a major player in the metabolism of numerous clinically important drugs, including many opioids. Opioid prodrugs, such as codeine and tramadol, are converted into their more active analgesic metabolites, morphine and O-desmethyltramadol, respectively, because of this enzyme. The genetic variations in the CYP2D6 gene are highly diverse and can be classified into: 1) Poor Metabolizers (PMs): These individuals have an activity score of 0 and possess two non-functional alleles. They are unable to effectively convert prodrugs into active metabolites, resulting in little to no analgesic effect from drugs like codeine and tramadol. CPIC guidelines provide a strong recommendation to avoid the use of these opioids in PMs [78]. 2) Ultrarapid Metabolizers (UMs): Defined by an activity score greater than 2.25, UMs have an increased copy number of the CYP2D6 gene. They rapidly convert prodrugs to active metabolites, leading to higher-than-expected systemic levels of the active form. This significantly increases their risk of toxicity, including life-threatening respiratory depression. The FDA has added a boxed warning to codeine and tramadol products, contraindicating their use in children under 12, as reported cases of toxicity, including death, have been linked to the UM phenotype.

Normal and Intermediate Metabolizers.

These groups have expected or reduced enzyme activity, respectively. Normal metabolizers (activity score 1.25-2.25)

can be prescribed label-recommended dosing. Intermediate metabolizers (activity score 0-1.25) may have a less-than-optimal response to codeine or tramadol due to reduced morphine formation, and close monitoring or an alternative analgesic may be warranted.

The OPRM1 gene encodes the mu opioid receptor, which is the primary molecular target for opioids such as morphine, fentanyl, and methadone. Genetic variants within this gene can alter the function and expression of the receptor, and influence a patient's pain sensitivity, analgesic response, and vulnerability to opioid dependence. Although the evidence can be conflicting, this variant has been associated with opioid and alcohol addiction and variations in pain sensitivity. Patients with dysfunctional CYP2D6 or OPRM1 are considered high-risk (approximately 14% of the population) and are best managed with non-opioid therapies. Medium-risk patients (approximately 48%) with subnormal function can be managed with dose monitoring, while low-risk patients (approximately 38%) with functional genes are considered good candidates for standard opioid therapy [78]. The clinical utility of genetic information in guiding opioid therapy is not uniform across the entire drug class. While the evidence for codeine and tramadol, is sufficiently robust to support strong, actionable clinical guidelines, the data for other commonly used opioids, such as oxycodone and methadone, are significantly weaker or conflicting.

VTE- There is a significant genetic component that contributes to an individual's risk of suffering from VTE aside from the traditional clinical factors like age, obesity, and history. These include the Factor V Leiden (FVL) mutation and the prothrombin G20210A mutation [79]. The presence of either of these mutations approximately doubles the relative risk of a thrombotic event [80]. Polygenic risk scores (PRS) have emerged as a valuable tool for improving VTE risk assessment. Aggregating the cumulative weighted effect of numerous single-nucleotide polymorphisms (SNPs) across an individual's genome provides a single score that quantifies their overall genetic susceptibility, helping clinicians make more informed decisions. Including PRS, and more broadly genetics, into risk prediction models could enhance the risk assessment, potentially provide higher quality predictions that are more accurate, and provide these more efficiently, potentially in an earlier stage of life, and it could enable the development of personalised strategies for minimizing the risk, or therapies to work on any existing abnormalities. In detail review of examples of such PRS assessment systems is too vast and beyond the scope of this current report, as in the most recent decade, a plethora of studies have consistently identified newer genetic mutations and factors that may affect VTE risk [81-83].

SSI- The genetic predisposition to poor wound healing and surgical site infections (SSI) is a critical area for genetic-guided therapeutic decisions in the postoperative period. While it is true that such infections are primarily caused by microbial contamination, it is also true that the host's ability to manage these infections and successfully heal the wound has a significant genetic component. For instance, specific regions on chromosomes 9 & 14 have been shown to be statistically significant for postoperative sepsis (POS) [84]. Research has identified several genetic factors that can influence wound

healing and scarring, such as MGF3, discovered by researchers at Ohio State University, USA. The MTHFR gene has been shown to impair wound healing by causing hyperhomocysteinemia, which can lead to systemic inflammation and disrupt proper hemostatic function. The heritability of wound healing has been estimated to be as high as 86% in mice, and specific patterns of human gene expression are linked to the onset and progression of wound healing.

Discussion.

The development and practical use of new biomarkers will significantly increase the accuracy of predicting anesthesia outcomes. Because the use of biomarkers will make it possible to identify patients at risk of perioperative complications in a timely manner; ultimately, it will facilitate the correct/timely implementation of necessary preventive interventions; The integrating pharmacogenomics knowledge and advances into anaesthesia care can significantly improve patient outcomes. The identification of genetic markers significantly enhances the efficacy and safety of anaesthesia. Thus, the field of anaesthesia is increasingly dependent on precision and personalised approaches, thereby significantly improving patient safety. A greater focus on personalised approaches can be achieved by fully incorporating pharmacogenomics; it is precisely based on the patient's genetic characteristics that individualised treatment plans can be developed. Identifying specific genetic markers that affect drug metabolism and efficacy will enable clinicians to enhance the effectiveness and safety of anaesthetic care. Accordingly, the transition from a generic approach to a more tailored strategy significantly reduces the risk of adverse drug reactions, while also contributing to and focusing on better therapeutic outcomes. Overall, it contributes to patient recovery and a better prognosis. There is no doubt that integrating of both

nanotechnology and 3D printing in anaesthesia will significantly improve the development of personalised anaesthesia approaches, ultimately contributing to the development of effective and outcome-oriented treatment strategies. Thus, the combined use of the above-mentioned technologies will significantly improve the anaesthesia process and ultimately the development of patient-specific approaches (Figure 1).

Taken all together, pharmacogenomics can be considered the cornerstone of individualized anesthesia. Pharmacogenomics, the field that at the genetic level comprehends drug efficacy and its toxicity based on genetic variations affecting pharmacokinetics and pharmacodynamics, it can help guide the development of optimal therapeutic strategies [36]. And since there are variations in the way individual patients respond to anesthesia, pharmacogenomics plays a crucial role in identifying causative factors and developing efficient personalized anesthesia care. Furthermore, the way a person responds to drugs is dependent on the drug-metabolizing enzymes and their genetic variations, which are capable of activating and breaking down the drugs. Drug-metabolizing enzymes play a role in converting proactive drugs to their usable-active form in the body, however any genetic mutation or deficiency in these enzymes can affect this conversion leading to drug ineffectiveness and those drugs that are not capable of breaking down can lead to accumulation and then result in drug-toxicity and it's adverse side effects, which is why genetic variants are considered a crucial information in anesthesia care [37]. One such dominant drug-metabolizing enzyme is Cytochrome P450.

Cytochrome P450 (CYP450) belongs to a superfamily of enzymes, specifically the group B cytochromes, and is responsible for the metabolism of drugs, steroids and fatty acids. This group of enzymes includes NADPH cytochrome C reductase (flavoprotein), phosphatidylcholine (phospholipids)

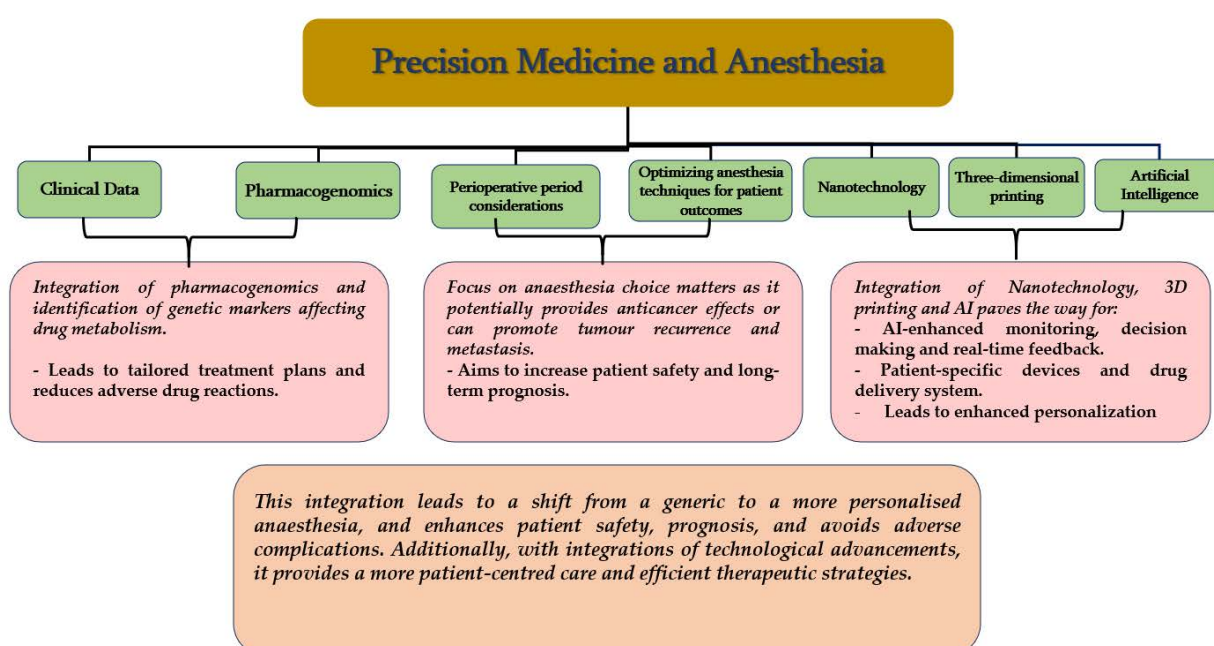


Figure 1. The significance of precision medicine in Anaesthesia.

and P450 (haemoglobin). Cytochrome P450, although found in cells of lungs, brain, kidneys, gastrointestinal tract, placental tissue and skin, is present in higher concentrations in the liver [85]. There are 57 isozymes, and six of these isozymes are responsible for 90% of drug metabolism, and those six isozymes are CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP2E1 and CYP3A4 [86]. Different drugs act on specific isozymes, and understanding which isozymes are targeted is essential for effective drug development [87]. Genetic polymorphisms can significantly influence how the CYP proteins metabolize drugs. Poor metabolizers can either reduce or eliminate enzyme activity, leading to increased drug levels and a higher risk of toxicity, while rapid metabolizers cause increased enzyme activity, resulting in rapid drug clearance and reduced drug efficacy [88]. To conclude, understanding pharmacogenomics, particularly CYP450 genetic polymorphisms, is essential for precision anesthesia. Furthermore, integrating gene-level data into preoperative planning can help anesthesiologists improve efficacy, minimize adverse complications, and provide optimal personalized patient care.

Thus, cutting-edge technologies facilitate is essential in precision medicine. In recent years, precision medicine has focused on tailoring medical treatment based on an individual's genetic profile, lifestyle, and environment. Many technological advances have been helping the field of personalized care to develop further. A few such advancements are artificial intelligence, nanotechnology, and three-dimensional learning.

Artificial Intelligence (AI), with its formidable data processing and self-learning capabilities, has enhanced monitoring in anesthesiology. Additionally, AI is capable of integrating with other technologies, such as electroencephalography (EEG) and near-infrared spectroscopy (NIRS), which helps receive real-time data and optimize patient care. Furthermore, AI enables genomic data analysis, predictive modelling, and decision support systems, and can further integrate with electronic health records, providing easy access for the healthcare workers [89,90].

The application of nanotechnology in medicine is closely related to the development of drug delivery systems within the body. Nanotechnology, specifically nanomedicine, is a pivotal technological advancement in recent years due to its ability to provide a targeted drug delivery system, which in turn can lead to improved therapeutic efficacy and minimize systemic side effects, highlighting its significance in precision medicine and anesthesia [60]. It is especially advantageous when it comes to the slow drug release effect of the medications used, which also includes anesthetics. Certain anesthetics in patients with a genetic predisposition can cause rapid metabolism and a higher drug clearance rate. In such cases, this property of nanoparticles becomes advantageous [91]. Anesthesiologist can utilize nanotechnology in routine clinical anesthesia and pain management to improve perioperative care and reduce perioperative-related complications [64,65].

Three-dimensional printing technology is one of the most recent technological advancements found in a broad range of areas, including both medical science and industrial fields. It is a type of manufacturing technology that involves easily accessible and modifiable digital structuring, utilizing bondable materials

such as plastics, polymers, and metals for manufacturing [66]. Additionally, it provides clinicians with tactile models derived from patient-specific pathology, enabling better understanding and simulation of complications. It is beneficial for both patient assessment and training due to its modifiability, cost-effectiveness, and rapid production [67,68]. Furthermore, 3D printing is used in the development of affordable and sustainable anesthesia equipment, such as thermal laryngoscopes. Its speed, adaptability, and economic feasibility make it a valuable tool in precision medicine and personalized anesthesia [69].

Therefore, the integration of artificial intelligence, nanotechnology, and three-dimensional printing creates great potential in optimizing preoperative care, personalized therapeutic strategies, and prevention of adverse risks. The integrating precision medicine/pharmacogenomics into anesthesiology is a crucial step in enhancing patient care. In particular, the maximum utilization of genomic data is beneficial for considering environmental and genetic factors that affect drug metabolism/efficacy. Healthcare professionals are given greater opportunities to develop individual anesthetic approaches that will significantly improve patient safety and therapeutic outcomes. Drug side effects will be significantly reduced, especially in patients with comorbidities, thereby ensuring the optimization of both intraoperative and postoperative care. Thus, the use of personalized strategies will be crucial in supporting anesthetic practice. Ultimately, it will contribute to improving patient outcomes in surgery and anesthesia. Precision medicine in anesthesiology aims to tailor anesthesia care to individual patient characteristics; however, its implementation faces significant challenges and presents promising opportunities. There are several key obstacles: integration of Advanced Technologies, Data Complexity and Standardization, Cost and Accessibility, and Ethical Concerns, among others. But it has tremendous Opportunities; particularly the decision based on the advanced monitoring technologies drives precise Decision Support, promising safer, more effective anesthesia.

Conclusion.

Pharmacogenomics, nanotechnology, three-dimensional printing technology, AI hold potential to transform precision anaesthesia, and it can enhance perioperative care by providing patient-centred drug delivery systems, customised surgical tools and improved therapeutic outcomes personalised to patients' needs.

REFERENCES

1. Gelb A.W, Morriss W.W, Johnson W, et al. World Health Organization-World Federation of Societies of Anaesthesiologists (WHO-WFSA) International Standards for a Safe Practice of Anesthesia. *Anesthesia and Analgesia*. 2018;126:2047-2055.
2. Harfaoui W, Alilou M, El Adib AR, et al. Patient Safety in Anesthesiology: Progress, Challenges, and Prospects. *Cureus*. 2024;16:e69540.
3. Howell S.J, Thompson J.P, Irwin M.G. Current challenges in vascular anaesthesia. *British Journal of Anaesthesia*. 2016;117:ii1-ii2.

4. Dutton R.P, Isaak R, Cammarata B.J, et al. The Future of Anesthesia Practice. *Advances in Anesthesia*. 2019;37:111-126.
5. Chin H, Ingerman Å, Block L, et al. Navigating the complex dynamics of anesthesiologists' professional identity formation in the context of their specialty training program: a phenomenographic perspective. *BMC Medical Education*. 2024;24:539.
6. Waisel D.B. The Role of World War II and the European Theater of Operations in the Development of Anesthesiology as a Physician Specialty in the USA. *Anesthesiology*. 2001;94:907-914.
7. White P.F, Kehlet H, Neal J.M, et al. The Role of the Anesthesiologist in Fast-Track Surgery: From Multimodal Analgesia to Perioperative Medical Care. *Anesthesia and Analgesia*. 2007;104:1380-1396.
8. Lark Amoa L.D, Mensah B, Sutari Y. Pharmacogenomics in Anesthesia: Tailoring Anesthetic Agents to Genetic Variations. *J Surgical Case Reports and Images*. 2025;8:2690-1897.
9. Ngcobo N.N. Influence of Ageing on the Pharmacodynamics and Pharmacokinetics of Chronically Administered Medicines in Geriatric Patients: A Review. *Clinical Pharmacokinetics*. 2025;64:335-367.
10. Johnson K.B, Wei W-Qi, Weeraratne D, et al. Precision Medicine, AI, and the Future of Personalized Health Care. *Clinical and Translational Science*. 2021;14:86-93.
11. Pot M, Spalletta O, Green S. Precision medicine in primary care: How GPs envision 'old' and 'new' forms of personalization. *Social Science & Medicine*. 2024;358:117259.
12. Jalilian L, Cannesson M. Precision Medicine in Anesthesiology. *International Anesthesiology Clinics*. 2020;58:17-22.
13. Berger-Estilita J, Marcolino I, Radtke F.M. Patient-centered precision care in anaesthesia – the PC-square (PC)² approach. *Current Opinion in Anaesthesiology*. 2024;37:163-170.
14. Ho D, Quake SR, McCabe ERB, et al. Enabling technologies for personalized and precision medicine. *Trends in Biotechnology*. 2020;38:497-518.
15. Xu W, Suo Z, Qu Y, et al. Retrospective and prospective: insights from a decade of anesthesiology trends for perioperative health care. *Frontiers in Medicine*. 2025;12:547487.
16. Taylor C, Crosby I, Yip V, et al. A Review of the Important Role of CYP2D6 in Pharmacogenomics. *Genes*. 2020;11:1295.
17. Fei Q, Zhang Y, Liu C, et al. Artificial intelligence in anesthesia and perioperative medicine. *Anesthesiology and Perioperative Science*. 2025;3:24.
18. Parada-Márquez J, Maldonado-Rodriguez N, Triana-Fonseca P, et al. Pharmacogenomic profile of actionable molecular variants related to drugs commonly used in anesthesia: WES analysis reveals new mutations. *Frontiers in Pharmacology*. 2025;14.
19. Abraham J, Bartek B, Meng A, et al. Integrating machine learning predictions for perioperative risk management: Towards an empirical design of a flexible-standardized risk assessment tool. *Journal of Biomedical Informatics*. 2023;137:104270.
20. Chau A, Ehrenfeld J.M. Using Real Time Clinical Decision Support to Improve Performance on Perioperative Quality and Process Measures. *Anesthesiology Clinics*. 2011;29:57-69.
21. Molla G, Bitew M. Revolutionizing Personalized Medicine: Synergy with Multi-Omics Data Generation, Main Hurdles, and Future Perspectives. *Biomedicine*. 2024;12:2750.
22. Erdmann A, Rehmann-Sutter C, Bozzaro C. Patients' and professionals' views related to ethical issues in precision medicine: a mixed research synthesis. *BMC Medical Ethics*. 2021;22:116.
23. Hazin R, Brothers KB, Malin BA, et al. Ethical, legal, and social implications of incorporating genomic information into electronic health records. *Genetics in Medicine*. 2013;15:810-816.
24. Kelsey M.D, Patrick-Lake B, Abdulai R, et al. Inclusion and Diversity in Clinical Trials: Actionable Steps to Drive Lasting Change. *Contemporary Clinical Trials*. 2022;116:106740.
25. L B. Pharmacogenomics in Anesthesia: Tailoring Anesthetic Agents to Genetic Variations. *Journal of Surgery Case Reports and Images*. 2025;8:01-06.
26. Belani K.G. Precision medicine and the expanding perioperative role by Anaesthesiologists. *Indian Journal of Anaesthesia*. 2025;69:745-747.
27. Arina P, Kaczorek MR, Hofmaenner DA, et al. Prediction of Complications and Prognostication in Perioperative Medicine: A Systematic Review and PROBAST Assessment of Machine Learning Tools. *Anesthesiology*. 2024;140:85-101.
28. Han L, Char D.S, Aghaeepour N. Artificial Intelligence in Perioperative Care: Opportunities and Challenges. *Anesthesiology*. 2024;141:379-387.
29. Kasztura M, Richard A, Bempong N-E, et al. Cost-effectiveness of precision medicine: a scoping review. *International Journal of Public Health*. 2019;64:1261-1271.
30. Ofori B, Twum S, Yeboah S.N, et al. Towards the development of cost-effective point-of-care diagnostic tools for poverty-related infectious diseases in sub-Saharan Africa. *Peer J*. 2024;12:e17198.
31. DiMaria S, Mangano N, Bruzzese A, et al. Genetic Variation and Sex-Based Differences: Current Considerations for Anesthetic Management. *Current Issues in Molecular Biology*. 2025;47.
32. Stefanicka-Wojtas D, Kurpas D. Personalised Medicine—Implementation to the Healthcare System in Europe (Focus Group Discussions). *Journal of Personalized Medicine*. 2023;13:380.
33. Upton D, Popovic K, Fulton R, et al. Anaesthetic-dependent changes in gene expression following acute and chronic exposure in the rodent brain. *Scientific Reports*. 2020;10.
34. Dorgalaleh A, Bahraini M, Ahmadi S. Personalized Anesthesia in Hematology. 2025;231-274.
35. Mohammadi-Yeganeh S, Bilanicz S, Dabbagh A. The Role of OMICS (Genomics, Epigenetics, Transcriptomics, Proteomics and Metabolomics) in Personalized Anesthesia and Perioperative Medicine. *Personalized Medicine in Anesthesia, Pain and Perioperative Medicine*. Springer International Publishing. 2021;9-63.
36. Bach-Rojecky L, Čutura T, Lozić M, et al. Personalized Anesthetic Pharmacology. In: Dabbagh A, editor. *Personalized Medicine in Anesthesia, Pain and Perioperative Medicine*. Cham: Springer International Publishing; 2021:65-92.

37. Duarte J.D, Cavallari L.H. Pharmacogenetics to guide cardiovascular drug therapy. *Nature Reviews Cardiology*. 2021;18:649-665.
38. Liu S, Zheng Q, Bai F. Differences of Atomic-Level Interactions between Midazolam and Two CYP Isoforms 3A4 and 3A5. *Molecules*. 2023;28:6900.
39. Wright W.C, Chenge J, Chen T. Structural perspectives of the CYP3A family and their small molecule modulators in drug metabolism. *Liver Research*. 2019;3:132-142.
40. Behrooz A. Pharmacogenetics and anaesthetic drugs: Implications for perioperative practice. *Annals of Medicine and Surgery*. 2015;4:470-474.
41. Roy J-N, Lajoie J, Zijenah LS, et al. CYP3A5 genetic polymorphisms in different ethnic populations. *Drug Metabolism and Disposition*. 2005;33:884-887.
42. Xia S, Zhou Di, Ge F, et al. Influence of Perioperative Anesthesia on Cancer Recurrence: from Basic Science to Clinical Practice. *Current Oncology Reports*. 2023;25:63-81.
43. Cheng Y, Wu Y, Xu L. Effects of anesthetics on development of gynecological cancer. *Frontiers in Cell and Developmental Biology*. 2025;13:1587548.
44. Choi H, Hwang W. Anesthetic Approaches and Their Impact on Cancer Recurrence and Metastasis: A Comprehensive Review. *Cancers*. 2024;16:4269.
45. Benzonana L.L, Perry NJS, Watts HR, et al. Isoflurane, a Commonly Used Volatile Anesthetic, Enhances Renal Cancer Growth and Malignant Potential via the Hypoxia-inducible Factor Cellular Signaling Pathway In Vitro. *Anesthesiology*. 2013;119:593-605.
46. Gray K, Adhikary S, Janicki P. Pharmacogenomics of analgesics in anesthesia practice: A current update of literature. *Journal of Anaesthesiology, Clinical Pharmacology*. 2018;4:155-160.
47. Kong Y, Yan T, Gong S, et al. Opioid receptor mu 1 (OPRM1) A118G polymorphism (rs1799971) and postoperative nausea and vomiting. *American Journal of Translational Research*. 2018;10:2764-2780.
48. Mikstacki A, Skrzypczak-Zielińska M, Tamowicz B, et al. The impact of genetic factors on response to anaesthetics. *Advances in medical sciences*. 2013;58:9-14.
49. Okolo D, Ugorji W.S, Gopep N.S, et al. Perioperative Management of Anesthesia in Patients with Cardiovascular Disease: A Review of Current Guidelines in the United States. *Cureus*. 2025.
50. Landau R, Bollag L.A, Kraft J.C. Pharmacogenetics and anaesthesia: the value of genetic profiling. *Anaesthesia*. 2012;67:165-179.
51. Ellinas H, Albrecht M.A. Malignant Hyperthermia Update. *Anesthesiology Clinics*. 2020;38:165-181.
52. Harrod K. Precision Medicine in Anesthesia: Genetic Component in Opioid-induced Respiratory Depression. *clinicaltrials.gov*. 2025.
53. Agrò F.E, Pilegio C, Rizzo S, et al. Personalized Cardiac Anesthesia. In: Dabbagh A, editor. *Personalized Medicine in Anesthesia, Pain and Perioperative Medicine*. Cham: Springer International Publishing. 2021:93-115.
54. Collett S, Massmann A, Petry NJ, et al. Metoprolol and CYP2D6: A Retrospective Cohort Study Evaluating Genotype-Based Outcomes. *Journal of Personalized Medicine*. 2023;13:416.
55. Shrivastava A, Haase T, Zeller T, et al. Biomarkers for Heart Failure Prognosis: Proteins, Genetic Scores and Non-coding RNAs. *Frontiers in Cardiovascular Medicine*. 2020.
56. Clinical evidence: Acumen Hypotension Prediction Index (HPI) Software. *Edwards Lifesciences*. 2025.
57. Daidone M, Ferrantelli S, Tuttolomondo A. Machine learning applications in stroke medicine: advancements, challenges, and future perspectives. *Neural Regeneration Research*. 2024;19:769-773.
58. Single nucleotide polymorphisms associated with the human electroencephalogram during desflurane anaesthesia. *University of Waikato*. 2025.
59. An J, Zhao L, Duan R, et al. Potential nanotherapeutic strategies for perioperative stroke. *CNS Neuroscience & Therapeutics*. 2022;28:510-520.
60. Bayda S, Adeel M, Tuccinardi T, et al. The History of Nanoscience and Nanotechnology: From Chemical–Physical Applications to Nanomedicine. *Molecules*. 2019;25:112.
61. Desai C, Koupenova M, Machlus K.R, et al. Beyond the thrombus: Platelet-inspired nanomedicine approaches in inflammation, immune response, and cancer. *Journal of Thrombosis and Haemostasis*. 2022;20:1523-1534.
62. Vahabi S, Eatemadi A. Nanoliposome encapsulated anesthetics for local anesthesia application. *Biomedicine & Pharmacotherapy*. 2017;86:1-7.
63. Ribeiro L.N.M, Franz-Montan M, Alcântara ACS, et al. Hybrid nanofilms as topical anesthetics for pain-free procedures in dentistry. *Scientific Reports*. 2020;10:11341.
64. Zhang S, Wang Y, Zhang S, et al. Emerging Anesthetic Nanomedicines: Current State and Challenges. *International Journal of Nanomedicine*. 2023;18:3913-3935.
65. Liu G-L, Bian W-C, Zhao P, et al. Delivery of Local Anesthesia: Current Strategies, Safety, and Future Prospects. *Current Drug Metabolism*. 2019;20:533-539.
66. Lehmann T, Rose D, Ranjbar E, et al. Large-scale metal additive manufacturing: a holistic review of the state of the art and challenges. *International Materials Reviews*. 2022;67:410-459.
67. Carter J.C, Broadbent J, Murphy E.C, et al. A three-dimensional (3D) printed paediatric trachea for airway management training. *Anaesthesia and Intensive Care*. 2020;48:243-245.
68. Han M, Portnova A.A, Lester M, et al. A do-it-yourself 3D-printed thoracic spine model for anesthesia resident simulation. *Plos One*. 2020;15:e0228665.
69. Dinsmore M, Doshi S, Sin V, et al. Design and evaluation of a novel and sustainable human-powered low-cost 3D printed thermal laryngoscope. *Journal of Medical Systems*. 2019;43:143.
70. Gu S, Luo Q, Wen C, et al. Application of Advanced Technologies—Nanotechnology, Genomics Technology, and 3D Printing Technology—In Precision Anesthesia: A Comprehensive Narrative Review. *Pharmaceutics*. 2023;15:2289.

71. Bellini V, Russo M, Domenichetti T, et al. Artificial Intelligence in Operating Room Management. *Journal of Medical Systems*. 2024;48:19.
72. Balavenkatasubramanian J, Kumar S, Sanjayan R.D. Artificial intelligence in regional anaesthesia. *Indian Journal of Anaesthesia*. 2024;68:100-104.
73. Yang L, Tautz T, Zhang S, et al. The current status of malignant hyperthermia. *Journal of Biomedical Research*. 2020;34:75.
74. Sangkuhl K, Dirksen R.T, Alvarellos M.L, et al. PharmGKB summary: very important pharmacogene information for CACNA1S. *Pharmacogenetics and Genomics*. 2020;30:34-44.
75. What genetic abnormality causes resistance to anesthesia and intolerance to pain medication (analgesics)? Droracle. 2025.
76. Rosenberg H, Sambuughin N, Riaz S, et al. Nonsyndromic Malignant Hyperthermia Susceptibility. In: *GeneReviews®*. Seattle (WA): University of Washington, Seattle; 1993. 2003.
77. Smith D.M, Weitzel K.W, Cavallari L.H, et al. Clinical Application of Pharmacogenetics in Pain Management. *Personalized Medicine*. 2018;15:117-126.
78. Ruano G. Fundamental Considerations for Genetically Guided Pain Management with Opioids Based on CYP2D6 and OPRM1 Polymorphisms. *Pain Physician*. 2018;21:E611-E621.
79. Goyal A, Hurjkalani S, Alexander K.M, et al. Role of polygenic risk scores in venous thromboembolism: current state and future directions. *Research and Practice in Thrombosis and Haemostasis*. 2025;9:102973.
80. Ringwald J, Berger A, Adler W, et al. Genetic Polymorphisms in Venous Thrombosis and Pulmonary Embolism After Total Hip Arthroplasty: A Pilot Study. *Clinical Orthopaedics and Related Research*. 2009;467:1507-1515.
81. Germain M, Chasman DI, de Haan H, et al. Meta-analysis of 65,734 Individuals Identifies TSPAN15 and SLC44A2 as Two Susceptibility Loci for Venous Thromboembolism. *American Journal of Human Genetics*. 2015;96:532-542.
82. Klarin D, Emdin C.A, Natarajan P, et al. Genetic Analysis of Venous Thromboembolism in UK Biobank Identifies the ZFPM2 Locus and Implicates Obesity as a Causal Risk Factor. *Circulation: Cardiovascular Genetics*. 2017;10:e001643.
83. Lindström S, Brody JA, Turman C, et al. A large-scale exome array analysis of venous thromboembolism. *Genetic Epidemiology*. 2019;43:449-457.
84. Ahmed K.S, Christensen MA, Bonde A, et al. Genomic analysis of surgical patients to identify patients at risk for postoperative sepsis and surgical site infection. *Journal of Trauma and Acute Care Surgery*. 2025;98:385-392.
85. Walton T.E, Desbruslais S.P. Omics and anaesthesia: pharmacogenomics, proteomics and metabolomics. *Anaesthesia & Intensive Care Medicine*. 2022;3:188-193.
86. Stavropoulou E, Pircalabioru G.G, Bezirtzoglou E. The Role of Cytochromes P450 in Infection. *Frontiers in Immunology*. 2018;9:89.
87. Nebert D.W, Russell D.W. Clinical importance of the cytochromes P450. *The Lancet*. 2002;360:1155-1162.
88. Vander Schaaf M, Luth K, M. Townsend D, et al. CYP3A4 drug metabolism considerations in pediatric pharmacotherapy. *Medicinal Chemistry Research*. 2024;33:2221-2235.
89. Hashimoto D.A, Witkowski E, Gao L, et al. Artificial Intelligence in Anesthesiology: Current Techniques, Clinical Applications, and Limitations. *Anesthesiology*. 2020;132:379-394.
90. Latifi K, Negaresh M, Javanshir N, et al. The Advent of Artificial Intelligence in Anesthesiology and Pain Management: A Review Article. *International Journal of Drug Research in Clinical Practice*. 2023;1:e14.
91. Lark Amoa L.D, Mensah B, Sutari Y. Pharmacogenomics in Anesthesia: Tailoring Anesthetic Agents to Genetic Variations. *J Surgical Case Reports and Images*. 2025;8:2690-1897.