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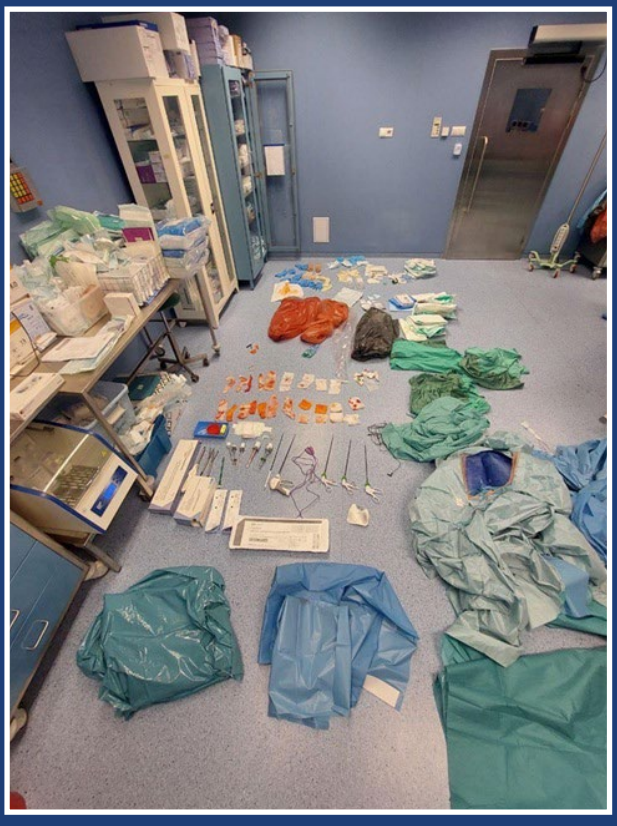

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Table of contents

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CASE REPORT

Acute appendicitis within an Amyand's hernia: a case report and literature review

Anita Krowiak[1,2,A–D], *Karolina Krowiak*[1,A,C–D], *Anna Maryńczak*[1,B–C], *Jakub Mendocha*[1,B,D], *Krzysztof A. Korneta*[1,3,E–F]

[1] Clinical Provincial Hospital No. 2 of St. Jadwiga the Queen, Rzeszów, Poland

[2] Department of Normal and Clinical Anatomy, Faculty of Medicine, Medical College of the University of Rzeszów, Poland

[3] Departament of Surgery, Faculty of Medicine, Medical College of the University of Rzeszów, Poland

A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

Abstract

Background: We present a clinical case of Amyand's hernia complicated by acute appendicitis.
Material and methods: A 71-year-old male presented with an incarcerated right inguinal hernia. Intraoperatively, a gangrenous, perforated appendix with associated purulent collection was identified, consistent with a type three Amyand's hernia.
Results: This case highlights the diagnostic and therapeutic challenges of Amyand's hernia. Due to its rarity and nonspecific presentation, the diagnosis is often made intraoperatively. Timely intervention and appropriate surgical strategy are essential to prevent complications.
Conclusions: Amyand's hernia should be considered in the differential diagnosis of complicated inguinal hernias. Surgical management must be adapted to the intraoperative findings.
Keywords: appendicitis, inguinal hernia, appendectomy, Amyand's hernia

Introduction

Amyand's hernia is a rare type of inguinal hernia, accounting for approximately 1% of all cases. The presence of acute appendicitis within the hernia sac is even more uncommon, observed in about 0.1% of hernias [1:329–336,2]. The diagnosis of this condition is both difficult and complex [3]. The main differential diagnoses include incarcerated intestinal loops, testicular inflammation, and testicular torsion, all of which may present with similar clinical features [4]. Prompt surgical intervention is essential in each of these conditions to prevent serious complications [5].

✉ Anita Krowiak, e-mail: krowiakanita@gmail.com

Case description

A 71-year-old patient was admitted on an emergency basis to the Department of General and Oncological Surgery due to an irreducible right inguinal hernia. Clinical examination revealed erythema of the inguinal region, along with swelling and redness of the right testicle. According to the patient's history, the hernia had been present for approximately two weeks, with increasing pain and swelling developing over the preceding two days.

The diagnostic tests performed in the Emergency Department included both laboratory and imaging tests. The laboratory results revealed significantly elevated inflammatory markers: the C-reactive protein (CRP) concentration was 279 mg/L (reference range <5 mg/L), the fibrinogen level was 9.94 g/L (reference range up to 4.0 g/L), and leukocytosis was present with a white blood cell (WBC) count of 16.41 × 10^3/μL (reference range <11.00 × 10^3/μL).

Abdominal radiography (X-ray) revealed the presence of single, short, nonspecific levels of fluid within the intestinal loops in the lower abdomen.

Abdominal ultrasonography demonstrated a right-sided inguinal hernia measuring approximately 50 × 35 × 96 mm, with a hernia orifice 20 mm in width. The hernia sac contained hyperechoic adipose tissue and a non-dilated intestinal loop with edematous and thickened walls, measuring up to 4.5 mm. A fluid collection of 22 × 10 mm was visualized in the anterior portion of the hernia sac. Additionally, small hyperechogenic foci consistent with the presence of gas were noted around the intestinal loop. The area was tender on palpation, clinically indicating signs of incarceration. On the left side, an inguinal hernia with a 14 mm orifice containing adipose tissue was also identified. During abdominal wall straining, transient protrusion of the intestinal loop into the hernia sac was observed. Due to the ultrasonographic confirmation of the intestinal loop within the hernia sac, along with clinical features suggestive of an incarcerated hernia, the decision was made to perform an urgent surgical intervention during the night. Computed tomography (CT) was not performed due to the urgency of surgical management aimed at preventing ischemic complications.

The emergency surgical procedure was performed under standard operating theatre conditions. After opening the anterior wall of the inguinal canal and carefully dissecting the incarcerated and inflamed hernia sac, the spermatic cord was isolated and the hernia orifice was exposed. Inside the hernia sac, an incarcerated, ischemic and gangrenous appendix was identified. Perforation was noted in both the body and the tip of the

organ. A purulent collection was also present. The intraoperative findings were consistent with an Amyand's hernia. The abscess was drained, and a specimen was collected for microbiological analysis. The appendix was removed retrogradely, with the stump secured using a ligature. Material was collected for histopathological examination. Furthermore, necrotic tissue surrounding the hernia sac up to its base was resected. Following this and after thorough irrigation of the surgical field, the inflammatory process remained localized within the hernia sac. As there were no indications for extending the surgical field, the peritoneal cavity was not explored to minimize the risk of spreading infection. In the subsequent stage of the procedure, the inguinal canal was reconstructed using the Bassini-Kirschner technique without synthetic materials. The spermatic cord was repositioned directly beneath the skin. Drainage was inserted using the Redon method. There were no indications for laparotomy or simultaneous repair of the left-sided inguinal hernia.

In the postoperative treatment, empirical combination antibiotic therapy, including clindamycin and metronidazole, was administered for two days until the microbiological culture results became available. Following identification of *Escherichia coli* in the culture, targeted antibiotic therapy with ciprofloxacin was initiated and continued for three days during hospitalization. After discharge, the patient was advised to continue taking ciprofloxacin, one tablet twice daily for seven days. Thromboprophylaxis was introduced early in the postoperative course. Follow-up laboratory results initially showed a slight increase in inflammatory markers, which significantly decreased after the initiation of targeted antibiotic therapy. Other laboratory parameters remained within normal limits. During hospitalization, the patient was evaluated by a cardiologist due to chronic coronary syndrome and a history of percutaneous coronary intervention (PCI). The postoperative course proceeded without complications.

The patient, in good general health, was discharged home after five days of hospitalization with recommendations for follow-up in the General Surgery Outpatient Clinic. As thromboprophylaxis, he received subcutaneous enoxaparin for five days following discharge. At follow-up visits, the postoperative wound demonstrated proper healing, with no abnormalities observed. He is currently awaiting elective repair of the left-sided inguinal hernia.

Discussion

Amyand's hernia is a rare condition defined by the presence of an appendix in the hernia sac. It was first described by Claudius Amyand in 1735,

when he performed an appendectomy on an 11-year-old boy, removing an inflamed appendix located in the inguinal hernia sac [1,5]. The incidence of this pathology is estimated at approximately 1% of all inguinal hernia cases, with only about 0.1% associated with appendicitis [2]. Amyand's hernia has been reported across a wide age range, from neonates to patients over 90 years old. Statistically, it occurs three times more frequently in children, which is thought to correlate with the persistence of a patent *processus vaginalis* in the pediatric population [6]. However, a more recent review, which includes publications from 2000 to 2019, demonstrated a reversal of this trend, with an observed increase among adults, who accounted for 57.5% of the group analyzed.

Moreover, the review confirmed a marked male predominance of the condition, accounting for 91% of those studied, and a higher prevalence of this type of hernia on the right side, observed in about 90.5% of cases [7].

The clinical manifestation of this disease is variable. The most common symptom is crampy, dull pain localized in the right lower quadrant, accompanied by an irreducible bulge of the abdominal wall in the inguinal or inguinoscrotal region. These symptoms typically suggest an incarcerated inguinal hernia, therefore appendicitis is rarely considered in the initial differential diagnosis [4]. In a case report presented by Chagam et al., it was emphasized that the coexistence of an incarcerated inguinal hernia with elevated inflammatory markers and decreased intestinal peristalsis should raise suspicion of the presence of an Amyand's hernia [8]. It confirms that these types of case pose a particular diagnostic and therapeutic challenge due to their nonspecific clinical presentation.

The imaging diagnosis of Amyand's hernia primarily relies on radiological investigations. Ultrasonography (USG) is the most commonly used method, although its effectiveness largely depends on the operator's experience. Diagnosis can be established by visualizing a blind-ended appendix within the hernia sac. However, in cases where inflammation is present, thickening of the appendix wall or obliteration of the surrounding fatty tissue may also be observed [3,9,10]. CT, with its higher sensitivity and specificity, allows direct visualization of the appendix in the inguinal canal and is therefore considered the diagnostic gold standard [3,11]. Both USG and CT are valuable diagnostic tools. However, in clinical practice, Amyand's hernia is often diagnosed only intraoperatively upon visualization of the appendix, whether normal or inflamed, within the hernia sac [12–14]. Furthermore, there are documented cases in which the condition was diagnosed incidentally during imaging performed for unrelated indications [15,16], as well as intraoperatively during routine inguinal hernia repair, despite preoperative ultrasonographic evaluation [17].

The current therapeutic approach to Amyand's hernia is primarily based on the evaluation of the condition of the appendix within the hernia sac. Losanoff and Basson devised a classification system that distinguishes four types of this pathology, depending on the severity of the inflammatory process and the presence of complications. Type one describes a hernia containing a normal, non-inflamed appendix. Type two involves a hernia with acute appendicitis, but without signs of sepsis. Type three includes cases with appendicitis accompanied by peritoneal or abdominal wall infection. The fourth type refers to the coexistence of appendicitis with other abdominal pathology [18].

The case presented here refers to a 71-year-old man with an incarcerated right inguinal hernia, in whom intraoperative findings revealed an ischemic, gangrenous appendix with perforation and a purulent focus. These findings confirmed the diagnosis of an Amyand's hernia, classified as type three according to the Losanoff and Basson's classification. Surgical management should be tailored to the condition of the appendix and intraoperative circumstances. In cases of appendicitis, a synthetic hernia mesh may be used if the surgical field is relatively clean. However, in the presence of abscesses, perforations, or extensive tissue infection, repair using the patient's tissues is recommended [7]. Following these recommendations, synthetic material was not used in the patient described, and hernia repair was performed with autologous tissues.

Conclusions

Amyand's hernia is a form of inguinal hernia rarely encountered in surgical practice, with preoperative diagnosis posing a significant clinical challenge. This case underscores the importance of maintaining diagnostic vigilance and considering a broad differential diagnosis in cases of incarcerated inguinal hernia, particularly when accompanied by signs of inflammation. Early surgical intervention, thorough assessment of anatomical conditions in the operative field, and accurate intraoperative diagnosis to guide optimal surgical technique, are crucial for improving prognosis and minimizing the risk of complications.

References

1. Amyand C. Of an inguinal rupture, with a pin in the appendix coeci, incrusted with stone; and some observations on wounds in the guts. *Philos Trans R Soc*. 1736;39:329–342.

2. Shaban Y, Elkbuli A, McKenney M, Boneva D. Amyand's hernia: A case report and review of the literature. *Int J Surg Case Rep*. 2018;47:92–96, https://doi.org/10.1016/j.ijscr.2018.04.034
3. Fezoulidi G, Argyrouli V, Adamopoulos E, Makridis KG, Zourntou S-E, Fezoulidis IV. Amyand's hernia: presumptive diagnosis by CT and literature review. *Radiol Case Rep*. 2021;16(4):911–915, https://doi.org/10.1016/j.radcr.2021.01.057
4. Sharma H, Gupta A, Shekhawat NS, Memon B, Memon MA. Amyand's hernia: a report of 18 consecutive patients over a 15-year period. *Hernia*. 2007;11(1):31–35, https://doi.org/10.1007/s10029-006-0153-8
5. Patoulias D, Kalogirou M, Patoulias I. Amyand's Hernia: an Up-to-Date Review of the Literature. *Acta Medica* (Hradec Kralove). 2017;60(3):131–134, https://doi.org/10.14712/18059694.2018.7
6. Ivanschuk G, Cesmebasi A, Sorenson EP, Blaak C, Loukas M, Tubbs SR. Amyand's hernia: a review. *Med Sci Monit*. 2014;20:140–146, https://doi.org/10.12659/MSM.889873
7. Manatakis DK, Tasis N, Antonopoulou MI, Anagnostopoulos P, Acheimastos V, Papageorgiou D, Fradelos E, Zoulamoglou M, Agalianos C, Tsiaoussis J, Xynos E. Revisiting Amyand's Hernia: A 20-Year Systematic Review. *World J Surg*. 2021;45(6):1763–1770, https://doi.org/10.1007/s00268-021-05983-y
8. Chagam L, Modi R, Toub F. Amyand's Hernia: A Rare Case Study of Perforated Appendicitis in an Inguinal Hernia. *Cureus*. 2024;16(3):e56898, https://doi.org/10.7759/cureus.56898
9. Guler I, Alkan E, Nayman A, Tolu I. Amyand's Hernia: Ultrasonography Findings. *J Emerg Med*. 2016;50(1):e15–e17, https://doi.org/10.1016/j.jemermed.2015.07.042
10. Chiang E, Belfer J, Baker MA, Ng L, Fenster D. Amyand Hernia: As Seen on Point-of-Care Emergency Ultrasound. *Pediatr Emerg Care*. 2022;38(3):e1087–e1089, https://doi.org/10.1097/PEC.0000000000002529
11. Holmes K, Guinn JE. Amyand hernia repair with mesh and appendectomy. *Surg Case Rep*. 2019;5(1):42, https://doi.org/10.1186/s40792-019-0600-2
12. Gao Y, Zhang T, Zhang M, Hu Z, Li Q, Zhang X. Amyand's hernia: a 10-year experience with 6 cases. *BMC Surg*. 2021;21(1):315, https://doi.org/10.1186/s12893-021-01306-z
13. Komorowski AL, Moran Rodriguez J. Amyand's hernia. Historical perspective and current considerations. *Acta Chir Belg*. 2009;109(4):563–564, https://doi.org/10.1080/00015458.2009.11680487

14. Aksędowski K, Komorowski AL, Bazielich AW, Sielski P. Strangulated epiplon in the inguinal canal as an atypical presentation of Amyand hernia. *M&PH*. 2023;1(1):1–4, https://doi.org/10.48269/MandPH-AF-MKU-23-1-005
15. Mohaidin N, Ong SCL. Incidental discovery of Amyand's hernia. *BMJ Case Rep*. 2018;2018:bcr2018227122, https://doi.org/10.1136/bcr-2018-227122
16. Resorlu M, Aylanç N, Karatag O, Ozturk MO. Amyand's hernia detected incidentally in two patients. *BMJ Case Rep*. 2017;2017:bcr2017221837. https://doi.org/10.1136/bcr-2017-221837
17. Katembo Sikakulya F, Kiyaka SM, Masereka R, Onyai P, Anyama P. Incidental discovery of Amyand's hernia in an adult female: A case report. *Int J Surg Case Rep*. 2021;83:106003, https://doi.org/10.1016/j.ijscr.2021.106003
18. Losanoff JE, Basson MD. Amyand hernia: a classification to improve management. *Hernia*. 2008;12(3):325–326, https://doi.org/10.1007/s10029-008-0331-y

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REVIEW PAPER

Operating room waste management after open and laparoscopic hepatectomy. Is there any possibility of improving it?

Magdalena Maria Wąsik[1,A,C–E], *Oleksii Potapov*[2,B–C,E], *Peter Sielski*[1,B–D], *Jarosław Kolendo*[3,B,E], *Stefania Marconi*[4,A,E], *Manuel Sanchez Casalongue*[5,C–D], *Andrzej L. Komorowski*[1,B,D–F]

[1] Medical College of the University of Rzeszów, Poland

[2] Department of General and Oncologic Surgery, District Hospital in Limanowa, Poland

[3] Zespół Przychodni Specjalistycznych w Tarnowie, Poland

[4] Univeristy of Pavia, Italy

[5] Clinica San Camilo, Buenos Aires, Argentina

A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

Abstract

Background: Operating rooms worldwide are one of the major sources of plastic waste. In this work we have speculated, that it is possible to limit the amount of waste produced during laparoscopic and open hepatectomies significantly, based on the analysis of single use items and the possibilities of replacing them with multiple use items. For this purpose, all waste produced during straightforward laparoscopic and open liver resections were analyzed, then divided into two groups: obligatory and non-obligatory waste.

Material and methods: During one open and one laparoscopic hepatectomy procedure, we have analyzed all waste produced as the result of the procedures. The waste was divided into two groups: obligatory and non-obligatory waste.

Results: All items used for each operation was separated from the waste bins after operation inside the OR. The members of the research team (M.W., O.P. and A.L.K) discussed each item and qualified it to one of the two categories: obligatory waste or non-obligatory waste. After assigning all waste items into one of the two groups, the non-obligatory waste was packed and weighted. The total weight and number of waste bins used for non-obligatory waste was recorded. Non-obligatory waste after laparoscopic hepatectomy weighted 3800 grams and was packed into two waste bins while after open hepatectomy the non-obligatory waste weighted 1400 grams and was packed into one waste bin.

Conclusions: Even a small reduction in cost of one procedure can translate globally into big savings for the hospitals and obviously for less environmental impact of the hospital waste.

Keywords: environment, laparoscopic hepatectomy, medical waste, open hepatectomy, operating room waste

✉ Maria Wąsik, e-mail: wasik.magdalena12@gmail.com

Introduction

Hospitals are a major source of waste throughout the world. In the USA alone, healthcare is the second largest waste contributor with over 4 billion tonnes of total waste production per year. Of this number, around 70% of all hospital waste is directly related to operating theatres (OTs) [1]. As medical professionals have become increasingly dependent on single-use instruments, this might be a moment to verify whether this dependency is always rational. If it were possible to limit the amount of waste produced during surgery, this could have a very positive impact on the environment [2]. There are also several indications that such an approach might help to limit costs for hospitals in two different ways: limiting the direct cost of medical supplies [3] and limiting the cost of waste management [2]. This paper concentrates on evaluating the extent to which we can limit operating theatre waste after open and laparoscopic liver resection by simply identifying those single-use items that can be easily replaced by multiple-use items.

Methods

During one open and one laparoscopic hepatectomy procedure, we analyzed all waste produced as the result of the procedures. The waste was divided into two groups: obligatory waste and non-obligatory waste. Non-obligatory waste was defined as single-use items that were opened by the scrub nurse but not used during surgery, single-use items that could have been replaced by multiple-use items and boxes of both types of items mentioned above. The possibility of replacement of a single-use item was defined as the current existence of a commercially available set of multiple-use items that could have been used instead of a single-use one (e.g. multiple-use trocars vs. single-use trocars) and not as a theoretical possibility of replacement (e.g. multiple-use surgical gloves).

Results

All items used for each operation were separated from the waste bins after the operation inside the OT. The members of the research team (M.W., O.P. and A.L.K) discussed each item and placed it into one of the two categories: obligatory waste or non-obligatory waste. After assigning all waste items to one of the two groups, the non-obligatory waste was packed and weighed (Figure 1). The total weight and number of waste bins used for non-obligatory waste were recorded. Non-obligatory waste after laparoscopic hepatectomy weighted 3800 grams and was packed into two waste

bins, while after open hepatectomy the non-obligatory waste weighted 1400 grams and was packed into one waste bin.

Discussion

Over the last few decades we have become accustomed to the ever-growing amount of waste produced by hospitals in general and by operating rooms specifically. The COVID-19 pandemic saw an even higher rate of growth of hospital waste, hopefully to a level that should prove to be a tipping point for us [4]. Many medical professionals realized that the continuous creation of ever higher mountains of medical waste is simply unsustainable in the long run.

Therefore, it is not surprising that opportunities to limit the amount of medical waste are being researched.

An obvious way to limit the total amount of plastic waste in the OT and at the same time to limit significantly the total cost of procedures is, if we so wish, to sterilize and reuse some single-use items. Tempting as it may sound, this strategy is, however, illegal in developed countries, mainly due to the risk of cross contamination [5].

Another simple step is to open only the single-use instruments that will be used during the operation. Once the sterile surgical supplies are opened, they will eventually become part of the OT waste even if they are not used. Hence, they should be opened only when necessary. Although it sounds obvious, it was shown that implementing this approach in a paediatric surgery OT can result in a average of nine items that are not used and not going to waste [6]. This approach is somewhat demanding, as the industry tends to prepare complete sets of single-use instruments for a certain type of surgery. When the possibility of putting together one's own sets of single-use instruments is researched, it may be beneficial in terms of reducing OT waste to eliminate some items from sets of prefabricated disposable items and instruments in order to reduce the total cost of plastic and hand surgery [3].

An important element of the strategy of hospital administrations is always the reduction of costs. Cutting down on the amount of waste can help lower costs in two ways: by directly limiting the cost of single-use items [3] and by lowering the cost of medical waste management [2]. A further result of the successful reduction of waste could be non-directly related to hospital costs. Most probably such an attitude would be considered a positive example of the social responsibility of the hospital management.

Throughout the world, the number of hepatic resections is growing, as is the amount of medical waste produced by HPB surgery. Between 1996

and 1997 in the USA 2097 liver resections were performed [7]. Similar numbers were obtained in the Netherlands (a country with a population roughly 20 times smaller than the USA) between 2014 and 2017 [8]. At the same time, the amount of waste associated with a single operation has also grown.

In the USA it is estimated that the cost of hospital waste management is around 2.36 USD per kg, and it is even higher for OT and ICU waste management at 5.96 USD [2]. While this price may seem modest, we have to consider that the total amount of medical waste produced by American hospitals is roughly 4 billion tonnes per year. This makes medical waste management a multi-billion-dollar business [1].

Conclusions

Even a small reduction in the cost of one procedure can translate globally into considerable savings for hospitals and, obviously, hospital waste has less impact on the environment.

It is naturally impossible to foresee the real impact of the approach proposed in this paper on the cost of hepatic resection, as ours is merely a feasibility study based on two cases. It seems, however, that there exists a significant margin of improvement for the management of OT waste after liver surgery. If we can confirm this via further studies, it may have a positive impact on the environment and at the same time help to reduce the costs of material and hospital waste management [Table 1,2].

Table 1. Details about open hepatectomy and laparoscopic hepatectomy

Surgery type	**Open hepatectomy**	**Laparoscopic hepatectomy**
Type of resection	resection of segment 7	bisegmentectomy s2–s3
Blood loss	100 ml	100 ml
Operating time	2h	2.5h
Transection	transection with single-use energy device and multiple-use bipolar device	transection with single-use energy device
Type of suction	re-usable suction device	single-use suction

Table 2. Differences between non-obligatory and obligatory waste

Non-obligatory waste	Obligatory waste
single-use items that were opened by the scrub nurse but not used during surgery	multiple-use items that were opened by the scrub nurse but not used during surgery
single-use items that could have been replaced by multiple-use items	single-use items that could not have been replaced by multiple-use items (e.g. surgical gloves, sutures)
coverage boxes for one-use items	coverage boxes for multiple-use items

Figure 1. Disposable operating theatre items

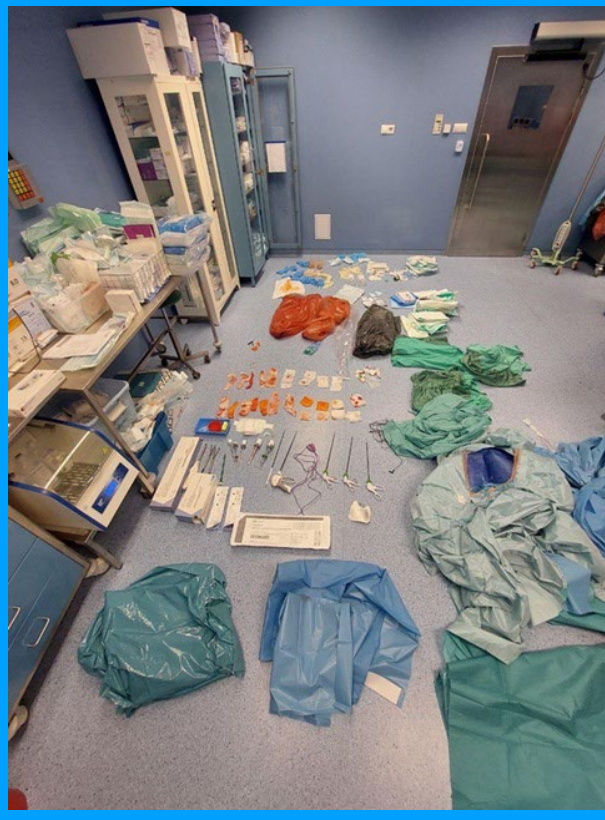

Photo by Oleksii Potapov

References

1. Kwakye G, Brat GA, Makary MA. Green surgical practices for health care. *Arch Surg*. 2011;146(2):131–136.
2. Vaccari M, Tudor T, Perteghella A. Costs associated with the management of waste from healthcare facilities: An analysis at national and site level. *Waste Manag Res*. 2017;36(1):39–47.
3. Albert MG, Rothkopf DM. Operating room waste reduction in plastic and hand surgery. *Plast Surg (Oakv)*. 2015;23(4):235–238.
4. Anstey MH, Trent L, Bhonagiri D, Hammond NE, Knowles S, McGain F; George Institute for Global Health and the Australian and New Zealand Intensive Care Society Clinical Trials Group; Steering Committee members; Coordinating centre List of investigators; Site List of investigators. How much do we throw away in the intensive care unit? An observational point prevalence study of Australian and New Zealand ICUs. *Crit Care Resusc*. 2023;25(2):78–83.
5. Favero MS. Requiem for reuse of single-use devices in US hospitals. *Infect Control Hospital Epidemiol*. 2001;22(9):539–541.
6. Goldfield NM, Malapati P, Chafitz T, Saravanapavan Y, Alamgir N, Gander J, Meyer MJ. Sterile surgical supply waste identification using asynchronous analysis: Pediatric surgery QI pilot. *Surg Open Sci*. 2023;15:32–37.
7. Dimick JB, Cowan JA Jr, Knol JA, Upchurch GR Jr. Hepatic Resection in the United States: Indications, Outcomes, and Hospital Procedural Volumes From a Nationally Representative Database. *Arch Surg*. 2003;138(2):185–191, https://doi.org/10.1001/archsurg.138.2.185
8. Olthof PB, Elfrink AKE, Marra E, Belt EJT, van den Boezem PB, Besscha K, Consten ECJ, den Dulk M, Gobardhan PD, Hagendoorn J, van Heek TNT, IJzermans JNM, Klaase JM, Kuhlmann KFD, Leclercq WKG, Liem MSL, Manusama ER, Marsman HA, Mieog JSD, Oosterling SJ, Patijn GA, Te Riele W, Swijnenburg R-J, Torrenga H, van Duijvendijk P, Vermaas M, Kok NFM, Grünhagen DJ; Dutch Hepato Biliary Audit Group. Volume-outcome relationship of liver surgery: a nationwide analysis. *Br J Surg*. 2020;107(7):917–926.

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REVIEW PAPER

Artificial Intelligence in Psychiatry: Assistant or Successor? – a review on the feasibility of replacing Psychiatrists with Artificial Intelligence

Katarzyna Wróblewska[A–F], *Julia Aleksandra Kożlak*[A–F], *Justyna Maria Hybel*[B–D]

[1] Medical College, Andrzej Frycz Modrzewski Krakow University

A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

Abstract

Background: This research aims to examine the potential of artificial intelligence (AI) within the field of psychiatry and to evaluate the potential for modern technologies to supplant psychiatric specialists in the future. Present applications of AI in the diagnosis, therapy and monitoring of patients are presented, considering both the advantages and limitations of these solutions. Ethical, social and legal aspects related to the employment of artificial intelligence in psychiatric care are also discussed.

Material and Methods: The paper is based on a review of the scientific literature. A total of 16 publications addressing the application of artificial intelligence in psychiatry were selected and examined using keywords related to artificial intelligence and psychiatry. Relevant studies were identified, and key concepts extracted, systematized, and analyzed to address the research objectives.

Results: Research on the use of artificial intelligence in psychiatry is limited and not yet fully explored, as the implementation of AI in medicine, particularly in psychiatry, remains a relatively new and developing field. The analyzed studies provide insight into current applications of AI in psychiatric diagnostics, therapy, and patient monitoring. Despite promising progress, the findings consistently emphasize that although AI offers valuable support in clinical practice, it cannot replace human psychiatrists, particularly in areas requiring empathy, emotional sensitivity, and complex interpersonal relationships.

Conclusions: Artificial intelligence can support psychiatrists in data analysis, early diagnosis, and personalized treatment, but it cannot replace the human element of empathy and patient care. Ethical and legal challenges also limit its full implementation, so AI should be viewed as a supportive tool rather than a substitute for specialists.

Keywords: artificial intelligence, clinical decision-making, psychiatry, artificial intelligence in medicine, future of psychiatry

✉ Katarzyna Wróblewska, e-mail: katarzyna.wroblewska00@outlook.com

Introduction

In recent years, artificial intelligence (AI) has become one of the most important trends in contemporary medicine, encompassing applications ranging from diagnostic imaging to clinical decision support. In the field of mental health, the development of AI is particularly noteworthy due to the increasing need for psychiatric services and the shortage of specialists. There are growing assertions that AI may eventually take over some of the duties of psychiatrists, or even replace them entirely. However, before accepting such a possibility as plausible, it is essential to analyze not only the unquestionable benefits, but also the limitations of the technology.

Methodology

An extensive search on PubMed, Google Scholar, Science Direct, ClinicalKey and EBSCO was performed, using key terms, such as AI, machine learning (ML), artificial wisdom, psychotic disorders, affective disorders, autism spectrum disorder, therapeutic robots, biomarkers, advantages, disadvantages, limitations, future, risks, opinions. The search involved various permutations and combinations of terms. Relevant references were then selected, and information was collected from these sources as key concepts. These concepts were systematized and discussed.

Artificial intelligence

History of artificial intelligence

The history of AI can be traced back to the 1950s, when scientists began to investigate whether machines were capable of thinking like humans. In 1956, at the Dartmouth Conference, John McCarthy used the term "artificial intelligence", which is considered to be the beginning of this discipline. The initial years brought optimism as well as the first programmes, such as symbolic reasoning systems. Then the 1990s and 2000s introduced new advancements, including the victory of the Deep Blue computer over chess champion Garry Kasparov (1997) and the development of ML [1]. A breakthrough occurred in the era of deep learning during the 2010s, when computing power and data accessibility enabled AI to achieve remarkable successes, such as AlphaGo's win over the champion Go player (2016) [2]. Currently, AI is ubiquitous, ranging from speech recognition to autonomous vehicles and advanced data analysis.

Definitions

Artificial intelligence represents one of the most rapidly expanding and pervasive technologies in the world. Despite its growing significance, a singular, universally accepted definition has yet not been developed [3].

The first definition of AI was proposed by McCarthy in 1956. It defined AI as "the science and engineering of making intelligent machines" [4:2]. Nowadays AI is defined in various ways. One of the definitions of AI is "The imitation of all human intellectual abilities by computers" [3:20]. "[...] the computer scientist Nils John Nilsson describes a technology that 'functions appropriately and with foresight in its environment'. [...] A similar definition has been put forward by the High-Level Expert Group on Artificial Intelligence (AI HLEG) of the European Commission (EC): 'Systems that display intelligent behaviour by analysing their environment and taking actions – with some degree of autonomy – to achieve specific goals'" [3:16]. As technology and research in AI progress, its definition will continue to evolve, adapting to new developments and challenges.

Concepts

To gain a deeper understanding of AI and its capacity for making intricate decisions, it is essential to examine its operational procedures.

A fundamental element of AI is ML. This is a sub-discipline of AI that involves designing computer algorithms capable of automatically improving their performance based on experience. ML algorithms develop models based on training data: a collection of instances from which the system learns to recognize patterns, predict outcomes or make decisions [5].

One of the more advanced mechanisms is the neural network. A neural network is a form of supervised ML. In this mechanism, data passes through a sequence of interconnected neurons, which are responsible for weighing and modifying information at every phase of analysis. The neural networks allow conclusions to be drawn from intricate and ostensibly unrelated data, rendering an exceptionally potent instrument for tasks including image recognition, text analysis, and classification [5].

A more advanced approach is deep learning, which evolved from the development of artificial neural networks. Systems based on deep learning systems comprise three or more layers of neurons that facilitate the progressive extraction of increasingly sophisticated features from the original input data. This makes it possible to generate results categorized or predicted with greater precision [5].

Core mechanisms such as ML, neural networks, and deep learning form the foundation of contemporary AI. Their ability to analyze complex datasets has enabled their widespread use across numerous disciplines, particularly in healthcare and psychiatry, where they support diagnosis, treatment planning and patient monitoring. The following section explores the growing influence of AI in clinical practice.

Artificial intelligence in medicine

Artificial intelligence is assuming an increasingly significant role in medicine, revolutionizing the way diagnosis, treatment and healthcare management are implemented. Through advanced algorithms and analysis of extensive data sets, AI is assisting doctors in making more precise judgments and enhancing medical outcomes. The application of AI is exerting a wide-ranging impact on diverse areas of medicine, including diagnosis, therapy, surgery and medical data management.

Diagnostics of diseases

One of the most significant applications of AI in medicine is disease diagnosis. Algorithms learnt from medical images demonstrate the ability to detect diseases, such as cancer, heart disease or tissue abnormalities, with a precision that frequently surpasses human diagnostic abilities. More specifically, the application of AI in the analysis of X-rays, CT scans or MRIs enables early detection of diseases, which is essential to the effectiveness of treatment [5].

Personalized therapy

Artificial intelligence significantly contributes to the healing process, especially in personalizing treatment. By analyzing medical data, including patients' medical histories and responses to various treatments, intelligent systems can customize treatment to meet the specific needs of particular patients. AI makes it possible to precisely select pharmaceuticals and optimize dosages, enhancing the effectiveness of therapy and minimizing the risk of side effects [1].

Medical data management

Artificial intelligence is also helping with medical data management. AI algorithms automate the analysis of patient records, which improves administrative work in hospitals and other healthcare institutions. Through the use of AI, medical information can also be better organized and processed, improving the efficiency of healthcare management [1].

Application of artificial intelligence in psychiatry

Mental disorders are a growing challenge for health care systems. According to the World Health Organization (WHO), depression is one of the leading causes of global disability, and the number of people suffering from anxiety disorders is consistently increasing [6]. In conventional psychiatry, diagnosis and therapies mainly rely on subjective clinical evaluations, which can lead to potential mistakes. AI offers a new approach, based on the analysis of multidimensional clinical data, allowing a more objective and precise assessment of the patient's condition.

Extraction and characterization of psychiatric features

Machine learning algorithms are being used to analyze psychiatric datasets, making it possible to identify significant traits of various mental disorders. By analyzing patient data, such as neuropsychological test results, clinical interview records, linguistic patterns and behavioural activity information, AI is able to detect subtle differences between different mental disorders. For instance, a study conducted by Dipnall et al. [7] involving over 5,500 patients with depression resulted in identifying over 250 biomarkers supporting accurate diagnosis [6,7]. Similarly, Abbas et al. [8] team used AI to analyze data on children at risk of autism spectrum disorder (ASD), which led to a significant enhancement in sensitivity and specificity of diagnosis compared to traditional screening techniques [6,8]. This application of AI enables earlier identification of disorders and better customization of therapeutic strategies to individual patients.

Detection of biomarkers in psychiatry

One of psychiatry's major challenges is the identification of objective biomarkers that can assist in the diagnosis and prognosis of mental illness. Psychiatric biomarkers can range from neurobiological indicators to behavioural or psychophysiological data. AI, in conjunction with neurobiological analysis, is opening up new possibilities in this area, by enabling more precise monitoring of changes in brain structure and function. For instance, research into Alzheimer's disease (AD) has used AI models to analyze magnetic resonance imaging (MRI) results. The established "AD pattern similarity score" enables a more precise evaluation of patients' cognitive function and prediction of disease risk. Moreover, AI algorithms are being used to analyze electroencephalographic (EEG) recordings to detect subtle patterns of neuronal activity associated with depression, schizophrenia or bipolar affective disorder, among others [6,9]. This approach not only

increases the efficiency of diagnosis, but also makes it possible to predict patients' responses to particular therapies.

Real-time monitoring and automated interventions

Contemporary AI technologies are supporting the development of real-time mental health monitoring instruments. The use of mobile devices makes it possible to collect behavioural and psychophysiological data, allowing for real-time tracking of a patient's mental state and early detection of deterioration. For example, the MindLAMP app analyzes data from questionnaires, cognitive tests and activity sensors [6]. AI algorithms can analyze changes in sleep habits, physical activity levels or communication patterns, so that patients and therapists can automatically receive alerts of potential risks of relapse. Moreover, technologies for facial recognition, speech analysis and activity patterns can support the diagnosis and treatment of disorders such as depression, schizophrenia, ADHD, ASD and addiction disorder. AI systems can also predict psychotic episodes or depressive relapses based on analysis of patients' behavioural patterns, providing the opportunity to implement interventions at an early stage.

Therapeutic robots and digital interventions

Artificial intelligence is also finding applications in modern forms of therapy, such as therapeutic robots. These robots are capable of performing actions of psychological support and assisting traditional treatments by analyzing patient interactions. For instance, a robot Woebot, an AI-based chatbot that employs natural language processing (NLP) algorithms, is programmed to conduct therapeutic conversations. Woebot analyzes patients' emotional state, to monitor mood and support cognitive-behavioral therapy (CBT). Other therapy robots, such as Nao and Kaspar, are designed to support therapy for children with ASD. With the ability to interact in a predictable and repetitive manner, they help children develop social and emotional skills. Kaspar uses simple gestures and speech to teach communication, while Nao helps develop interpersonal skills through play [6]. Research indicates that such solutions might increase patient engagement in therapy and improve its effectiveness. Furthermore, AI is being used to create virtual therapists and platforms to support CBT, making psychological help more accessible to people who have difficulty receiving traditional care.

Artificial intelligence in the management of mental disorders

Mood disorders: depression and bipolar affective disorder

Major depressive disorder (MDD) and bipolar disorder (BD) are among the most commonly diagnosed mental disorders. Due to the subjective nature of diagnosis, misdiagnoses are common – as many as 60% of BD cases are initially misclassified as MDD, resulting in a delay in appropriate treatment by an average of 10 years. AI is helping to improve diagnostic accuracy through the use of genomic analysis and neuroimaging methods. A study by Sun et al. used deep learning algorithms to analyze genetic variants in psychiatric patients, effectively distinguishing healthy individuals from depressed patients. Furthermore, Rubin-Falcone's research showed that the use of MRI and support vector machine algorithms can accurately distinguish MDD from BD. With these methods, AI can improve diagnostic accuracy. AI also significantly contributes to therapy support and relapse prevention. Examples include mobile apps such as Woebot and Tess, which support patients in managing emotions and reducing symptoms of depression [6]. By monitoring users' behavioural patterns, AI algorithms can tailor interventions, increasing the effectiveness of psychological support.

Autism spectrum disorders (ASD)

Early diagnosis of autism is crucial for effective therapy, although conventional diagnostic methods frequently fall short. AI can be used to analyze neuroinflammatory pathways and genetic mutations associated with ASD, which increases the sensitivity and specificity of screening tests. Social robots, such as Kaspar, are increasingly used to help children in cultivating social skills [6]. These robots offer predictable and personalized interactions, so they can increase the effectiveness of therapy compared to traditional methods. However, the robots' restricted adaptability and the peril of technological dependency continue to pose substantial concerns.

Schizophrenia and psychotic disorders

Artificial intelligence supports both the early diagnosis of schizophrenia and forecasts its progression. ML algorithms are being used to analyze MRI data to distinguish schizophrenia patients from healthy individuals with high accuracy [6]. Furthermore, AI makes it possible to monitor relapse risk based on data from mobile devices, analyzing changes in patients' physical activity and sleep patterns. One of the therapeutic breakthroughs is avatar therapy, developed at the Institute of Psychiatry, Psychology & Neuroscience at King's College London. It is used for patients suffering from persistent

auditory hallucinations that do not resolve despite pharmacological treatment. As part of the therapy, patients, along with a therapist, create a computer avatar representing the voice from the hallucination – its manifestation, sound and speech content. During therapy sessions, the patient carries on conversations with the avatar, gradually learning to take control of it and weaken its influence. Clinical studies conducted on a group of 150 patients have shown significant effectiveness of this method. After 12 weeks, patients in the avatar therapy group experienced notable improvement, and in seven patients the hallucinations completely disappeared (compared to two people in the control group). The effects also persisted after 24 weeks, confirming the long-term effectiveness of the therapy [10].

Advantages and disadvantages of artificial intelligence

Advantages

Among the many advantages of integrating AI into psychiatry, one of the key benefits is the development of intelligent self-assessment systems. These systems, designed to monitor symptoms evolution, treatment progress and medication compliance, are helpful in supervising a patient's condition and assessing risks in a timely manner. AI models have tremendous clinical potential in selecting personalized treatment for patients. AI can convey the most suitable treatment by analyzing data related to a patient's diagnosis, preferences, and treatment progression [6].

The development of telemedicine, supported by AI-based tools, enables patients to receive psychiatric care without the need for physical presence at a medical facility. This solution is particularly important for those living in areas with limited access to specialists and for patients requiring immediate support [4,6]. AI is being used in various applications, chatbots and online platforms that provide patients with anonymity and unlimited access, enabling them to interact with mental health support systems.

A breakthrough in this field has been the use of chatbots in therapy sessions. Chatbots, based on advanced NLP algorithms, can provide patients with basic psychological support, monitor mood, and refer them to appropriate specialists when alarming symptoms are detected [6].

Disadvantages

Despite the many benefits, there are several significant risks associated with implementing AI in psychiatric care. One of the fundamental challenges of using AI is the lack of full transparency in the operation of the algorithms. The term "Black Box" used in the scientific literature, refers

to the fact that even creators of models based on deep ML cannot fully explain the rationale behind AI decision-making and therefore the mechanism by which AI would make a diagnosis is unknown [6,11]. This may result in misdiagnoses and unsuitable treatment measures, obstructing the rectification of errors. An instance is the deployment of Watson technology at UB Songdo Hospital in Mongolia, where the technology recommended a patient a drug contraindicated for his condition [11]. The issue of responsibility for mistakes made by AI in diagnosis remains unsettled.

The effectiveness of AI-based systems is predominantly contingent upon the quantity and quality of the data utilized in their training. An insufficient or unrepresentative sample may lead to the model's inability to adjust to real-world conditions – with the risk of under-fitting, on the one hand, and over-learning the model, on the other, limiting its ability to make accurate predictions based on new data. Attaining the right balance between these phenomena requires careful calibration and repeated testing of the model. Consequently, drawing definitive conclusions from small data sets is unjustifiable, as it poses a significant risk of inaccuracies and misrepresentation [6].

Artificial intelligence algorithms require large amounts of patient data to be processed, which raises significant data privacy concerns. Improper data management could lead to data leakage or unauthorized use. There is also a risk that AI will be used to manipulate data or unknowingly share confidential information [4,6].

Another risk is the potential over-attachment of patients to interaction with AI-based tools at the expense of traditional therapy sessions. Certain research suggest that psychiatric patients may prefer AI interviews due to the anonymity they offer and the absence of subjective assessments. The absence of perceived judgement may make patients feel more comfortable interacting with an algorithm than with a human professional [4,6]. This phenomenon may result in patients disengaging from professional engagement, thereby adversely affecting treatment quality, therapeutic outcomes, and the long-term capacity to cultivate healthy interpersonal relationships [12].

Limitations of AI use in psychiatry

Artificial intelligence is widely used in medicine, especially in disciplines such as radiology, cardiology and dermatology. Its effectiveness derives from its ability to analyze extensive data sets characterized by reproducibility and objectivity [1,13]. The application of AI in the field of psychiatry faces significant difficulties, which stem from the very nature of

psychiatry and the traits of its patients [13]. Principal obstacles include the subjectivity of the input data, its restricted availability and the frequent co-occurrence of various disorders.

One of the challenges of using AI in psychiatric diagnosis is the subjectivity and variability of clinical data. Diagnoses derived from the DSM classification are mainly based on clinically observable behaviours and heterogeneous symptoms. Patients sharing the same diagnosis may present different symptoms, both in terms of type and severity. Furthermore, many psychiatric disorders share common clinical features and overlap. The comorbidity of disorders is fraught with the risk of subjective bias, potentially resulting in misattribution of symptoms to specific diagnoses [13,14].

Psychiatric databases are small and not very standardized [1214]. These challenges arise from the diversity of data collection methods, individual differences among patients, and the lack of standardized, readily accessible datasets.

It is also important to note that the results contained in these databases are often generalized on an international scale, despite significant differences in the level of digitization and data collection quality between high-income countries and those with fewer resources. In highly developed countries, healthcare digitization is more advanced, resulting in a larger quantity and higher quality of data available for analysis. In contrast, in less developed countries, access to digital systems is limited, which leads to a lower representation of these populations in the databases. Consequently, cultural diversity and the unique characteristics of various populations may be reflected to varying degrees, which poses a risk that AI models based on such data may lack sensitivity to cultural and regional contexts – potentially affecting the accuracy of diagnoses and therapeutic recommendations. Currently, the main types of data are demographics, diagnoses, medications, procedures, self-report questionnaires and clinical visits notes [13]. Standardization of psychiatric information is a challenge, which significantly hinders effective teaching of AI models.

Emotions and relationships, and the application of artificial intelligence in psychiatry

Artificial intelligence lacks the ability to experience emotions or form interpersonal relationships the way humans do [6]. This is a feature that can be both beneficial and problematic in terms of its application in psychiatry.

On the one hand, AI systems are immune to human factors such as stress, fatigue or emotional involvement, eliminating the risk of errors due to the

mental strain on the specialist [4,6]. Moreover, the lack of subjective feelings enables AI to conduct patient interviews in an impartial and non-judgmental manner. AI can also analyze data systematically and quickly, allowing it to detect patterns in patients' behavior and better predict their mental state [6,15].

However, emotions play a key role in the therapeutic process [15]. Psychotherapy relies not only on the content of speech, but also on subtle emotional signals, such as tone of voice, facial expression and body language. A human therapist can read a patient's emotions and adjust their response in a way that enhances a therapeutic relationship [12]. AI, despite its advanced algorithms, is not able to feel emotions or spontaneously adjust to dynamic changes in a patient's emotional state the way human does. As a result, the patient may feel misunderstood, which, in some cases, can even lead to mental deterioration [15]. Emotions are also essential in establishing trust. Patients often expect the therapist to show empathy, which reinforces a sense of security and comfort. A lack of emotional responsiveness in AI can lead to a sense of distance and coldness in the interaction, which can undermine the effectiveness of therapy [12].

Future prospects – will artificial intelligence replace the specialist?

Artificial intelligence is undoubtedly one of the fastest growing technologies in the world, hence presenting novel opportunities within the psychiatric field. With the growing accessibility of medical data and the development of ML algorithms, questions are being raised about the future of the psychiatry profession and the possibility of AI replacing it. AI has the potential to revolutionize diagnosis and treatment of mental problems; but, can it entirely supplant medical specialists? The purpose of this article is to analyze why AI, despite its enormous potential, is unable to replace psychiatrists.

Patient-psychiatrist interactions: the role of empathy

Successful psychiatric practice relies on the therapeutic relationship between patient and psychiatrist. Although AI can analyze linguistic and behavioural patterns, it cannot establish an empathic relationship with the patient and will not replace direct contact with the psychiatrist [6,12,15]. Psychiatric interventions are based on interpersonal relationships, empathy and the ability to grasp the patient's unique subjective experience – competencies that are inaccessible to AI technology [12,15]. Intuition and the ability to understand emotions are essential in diagnosing mental disorders, making the psychiatrist a key part of the treatment process. It is in this aspect that human interaction remains irreplaceable.

The role of psychiatrists in managing crisis situations

Psychiatrists often face challenging and crisis situations that require the ability to make decisions rapidly and adapt. Psychiatrists not only provide treatment, but also act as emotional support for patients during difficult times, which requires understanding and appropriate responses to a patient's changing needs in real time. Although AI can help monitor symptoms and predict risks, it is incapable of making decisions in situations that require empathy, intuition and adaptability. AI is unable to provide the same level of support that is crucial in crisis situations [12,15].

Ethical and regulatory issues

The effectiveness of machine-learning algorithms in psychiatry faces significant challenges, such as their vulnerability to reproducing cognitive errors and biases contained in training data [6]. Systems based on black box models suffer from a lack of transparency, making it impossible to fully understand the decision-making process [6,11]. This poses a serious ethical and clinical problem, especially in psychiatry, where the consequences of diagnostic mistakes can have serious long-term effects on patients. Furthermore, the issue arises as to a patient's entitlement to contest an AI-generated diagnosis and the appropriate procedures for such a challenge [11].

Automated AI-based systems also pose serious risks related to patient data privacy. AI systems are vulnerable to various forms of cyber threats, including hacking attacks that may lead to exposure of medical data [6,15]. Such incidents have serious repercussions, not only legally and ethically, but also personally; they violate patient rights and can lead to unauthorized use of information. Data concerning psychiatric patients is exceptionally sensitive, and its revelation may undermine trust in the mental health system, dissuade treatment, and significantly impair quality of life.

The main issues requiring regulation are the lack of transparency in AI operation and the resulting difficulty in assigning responsibility for diagnostic errors, as well as the patient's right to challenge a diagnosis. Equally important is ensuring the patient's informed consent to the inclusion of AI systems in the clinical decision-making process [6,11]. Regulations concerning the use of personal data also remain unresolved, further complicating the implementation of AI in clinical practice. All these matters remain unregulated in many jurisdictions.

A breakthrough step in this area was taken by the European Union on August 1, 2024, when it adopted comprehensive legal frameworks regulating the use of AI. The new regulations classify AI systems according to the level of risk they pose to users: unacceptable risk, high risk, limited risk,

and minimal risk. According to these regulations, AI used in healthcare is classified as a high-risk system. This means that the use of such solutions requires a number of conditions to be met, including ensuring transparency, protection against errors and cyber threats, as well as guaranteeing human oversight over the decision-making process. To implement the principle of transparency, there is a requirment to disclose that the content was generated by an AI system and to publish summaries of copyrighted data used to train these systems. By comparison, in the United States, there are currently no federal regulations directly governing the use of AI – only the Food and Drug Administration (FDA) approves selected AI solutions as medical devices. In China, AI is actively promoted but it requires strict oversight – systems used in the medical sector must be registered and tested before deployment.

Trust in the patient-psychiatrist relationship

The trust that develops between patients and psychiatrists during treatment is one of the key aspects in the effectiveness of the psychiatric treatment process. This trust is the foundation of the therapeutic relationship, enabling the patient to open up about difficult topics, express emotions and grapple with deep, personal experiences. The connection that develops through such interaction creates a space for the shared search for solutions in the context of psychiatric challenges. AI, despite its advancement in complex human relationships, cannot fully meet these fundamental requirements [6,12].

Artificial intelligence as a future assistant to the psychiatrist

In the forthcoming years, AI is poised to become an integral part of psychiatric practice, acting as an intelligent assistant to support both the diagnostic and therapeutic processes. With the ability to process and integrate a variety of data sources – from brain imaging to digital mental health indicators to NLP – AI systems can contribute to significant improvements in diagnostic accuracy and personalization of treatment [6].

Virtual reality combined with AI algorithms can enable dynamic and adaptive therapeutic scenarios tailored to the individual needs of patients with anxiety disorders or PTSD. At the same time, the development of digital tools that monitor mental status in real time, based on data from mobile apps or wearable devices, opens the way for early intervention and continuous therapeutic surveillance [16].

AI can also assist psychiatrists in building predictive clinical models to identify the risk of mental disorders, forecast their progression and evaluate the effectiveness of interventions. In this context, NLP tools are gaining

particular relevance, enabling the detection of subtle changes in patients' language that may correlate with psychopathological conditions [6].

Simultaneously, AI can significantly increase the availability of psychiatric care in populations with limited access to specialists. Chatbots and digital assistants capable of initial mental status assessment, psychoeducation and basic emotional support could be valuable additions to traditional models of care. However, further data standardization, interdisciplinary collaboration, and the development of an ethical and regulatory framework for its use in clinical settings are needed for AI to serve as a trusted and safe assistant to psychiatrists [6,12].

Results

This article discusses a limited number of studies addressing the use of AI in psychiatry. A literature search was conducted across PubMed, Google Scholar, Science Direct, ClinicalKey, and EBSCO, focusing on publications from the years 2016 to 2025. The topic of the use of AI in psychiatry remains relatively new and underexplored, for instance, a search in PubMed using our selected keywords for the years 2016–2025 resulted in only 11 relevant results. Approximately 40 articles were initially reviewed. However, many of them repeated the same core content and frequently cited identical foundational studies. These overlaps, along with the tendency to draw similar conclusions and rely on shared theoretical assumptions, reflect the early developmental stage of AI implementation in psychiatry. As a result, 16 articles were selected as the most relevant and representative for addressing the research question posed in this paper. These articles provided insight into the current applications of AI in psychiatric diagnostics, therapy and patient monitoring. Despite being published over a span of several years, they consistently support the view that while AI offers valuable support in clinical practice, it cannot replace human psychiatrists.

Conclusion

Artificial intelligence holds significant potential in supporting psychiatrists, especially in data analysis, early diagnosis and treatment personalization. However, the findings of this review indicate that although AI can meaningfully enhance psychiatric practice, it cannot replace the human element essential to empathy and patient relationships. Ethical and legal challenges also limit its full implementation. AI should be seen as a supportive tool, not a substitute for a specialist.

Declaration

This article was prepared with the assistance of artificial intelligence. AI-based tools were used for language editing and grammatical correction. All core ideas, analytical reasoning, and intellectual input were conceived and developed independently by the authors.

References

1. Patrzyk S, Woźniacka A. *Sztuczna inteligencja w medycynie*. Wydawnictwo Uniwersytetu Medycznego w Łodzi, Łódź 2022.
2. Silver D, Huang A, Maddison CJ, Guez A, Sifre L, et al. Mastering the game of Go with deep neural networks and tree search. *Nature*. 2016;529(7587):484–489, https://doi.org/10.1038/nature16961
3. Sheikh H, Prins C, Schrijvers E. Artificial Intelligence: Definition and Background. In: *Mission AI. The New System Technology*. Springer, Cham 2023, https://doi.org/10.1007/978-3-031-21448-6_2
4. Ray A, Bhardwaj A, Malik YK, Singh S, Gupta R. Artificial intelligence and psychiatry: an overview. *Asian J Psychiatr*. 2022;70:103021, https://doi.org/10.1016/j.ajp.2022.103021
5. Niewęgłowski K, Wilczek N, Madoń B, Palmi J, Wasyluk M. Zastosowania sztucznej inteligencji (AI) w medycynie. *Med Og Nauk Zdr*. 2021;27(3):213–219, https://doi.org/10.26444/monz/142085
6. Sun J, Dong Q-X, Wang S-W, Zheng Y-B, Liu X-X, et al. Artificial intelligence in psychiatry research, diagnosis, and therapy. *Asian J Psychiatry*. 2023;87:103705, https://doi.org/10.1016/j.ajp.2023.103705
7. Dipnall JF, Pasco JA, Berk M, Williams LJ, Dodd S, Jacka FN, Meyer D. Fusing data mining, machine learning and traditional statistics to detect biomarkers associated with depression. *PLoS One*. 2016;11(2):e0148195, https://doi.org/10.1371/journal.pone.0148195
8. Abbas H, Garberson F, Glover E, Wall DP. Machine learning approach for early detection of autism by combining questionnaire and home video screening. *J Am Med Inform Assoc*. 2018;25(8):1000–1007, https://doi.org/10.1093/jamia/ocy039
9. Casanova R, Barnard RT, Gaussoin SA, Saldana S, Hayden KM,. Using high-dimensional machine learning methods to estimate an anatomical risk factor for Alzheimer's disease across imaging databases. *Neuroimage*. 2018;183:401–411, https://doi.org/10.1016/j.neuroimage.2018.08.040
10. Craig TKJ, Rus-Calafell M, Ward T, Leff JP, Huckvale M, et al. AVATAR therapy for auditory verbal hallucinations in people with

psychosis: a single-blind, randomised controlled trial. *Lancet Psychiatry*. 2018;5(1):31–40, https://doi.org/10.1016/S2215-0366(17)30427-3
11. Xu H, Shuttleworth KMJ. Medical artificial intelligence and the black box problem: a view based on the ethical principle of "do no harm". *Intell Med*. 2024;4(1):52–57, https://doi.org/10.1016/j.imed.2023.08.001
12. Brown C, Story GW, Mourão-Miranda J, Baker JT. Will artificial intelligence eventually replace psychiatrists? *Br J Psychiatry*. 2021;218(3):131–134, https://doi.org/10.1192/bjp.2019.245
13. Rocheteau E. On the role of artificial intelligence in psychiatry. *Br J Psychiatry*. 2023;222(2):54–57, https://doi.org/10.1192/bjp.2022.132
14. Yan WJ, Ruan QN, Jiang K. Challenges for artificial intelligence in recognizing mental disorders. *Diagnostics* (Basel). 2023;13(1):2, https://doi.org/10.3390/diagnostics13010002
15. Blease C, Locher C, Leon-Carlyle M, Doraiswamy M. Artificial intelligence and the future of psychiatry: Qualitative findings from a global physician survey. *Digit Health*. 2020;6, https://doi.org/10.1177/2055207620968355
16. Torous J, Bucci S, Bell IH, Kessing LV, Faurholt-Jepsen M, et al. The growing field of digital psychiatry: current evidence and the future of apps, social media, chatbots, and virtual reality. *World Psychiatry*. 2021;20(3):318–335, https://doi.org/10.1002/wps.20883

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ORIGINAL RESEARCH PAPER

Very advanced maternal age – chance of pregnancy after ICSI

Jakub Wyroba[1,2,A–B,D,F], *Katarzyna Kostarczyk*[3,C–F], *Joanna Kochan*[1,3,B–D], *Alicja Lachowska*[1,B,E]

[1] Malopolski Institute of Fertility Diagnostics and Treatment – KrakOvi, Krakow, Poland

[2] Fertility Disorders Clinic, Medical College, Andrzej Frycz Modrzewski Krakow University, Poland

[3] Department of Animal Reproduction, Anatomy and Genomics, University of Agriculture in Krakow, Poland

A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

Abstract

Background: Postponing procreation becomes an increasing problem in developed countries. Maternal aging contributes to intensive development of assisted reproduction techniques (ART). The aim of the study was to analyze the results of in vitro fertilization in women of very advanced maternal age (AMA, ≥42Y) using autologous oocytes (AO) or donor oocytes (DO) compared to women ≤35Y.

Material and methods: This was a retrospective study of AMA women who underwent intracytoplasmic sperm injection (ICSI) using AO or DO. The control group consisted of young patients with age ≤35Y.

Results: In group of AMA patients, the AMH level was significantly lower (0.56 ng/ml) than in young patients (3.6 ng/ml), which corresponded to obtaining a significantly lower number of oocytes (1.6±0.4 vs 12±4 oocytes/cycle), ($p < 0.001$). In older patients with AO only 0.4±0.1 blastocysts/cycle were obtained compared to 1.9±0.7 when DO were used and 3.8±1.1 from young women. Euploidy rate of blastocysts obtained after fertilization of AO of AMA patients was 26% in compare to 57% in a group of young women and 54% in the group of older patients with DO. The implantation rate was significantly lower in the group of older patients with AO (28%) compared to the other groups (50%, 59%), ($p < 0.001$).

Conclusions: AMA patients must be aware that IVF procedure does not guarantee pregnancy and the birth of a healthy child and they should be offered pre-implantation PGT-A diagnostics due to the high risk of chromosomal defects. These patients should also be informed about the much higher effectiveness of IVF using DO.

Keywords: advanced maternal age, IVF, ART, reproductive aging, oocyte donation

Introduction

Recently, in high-income countries, there has been a tendency to delay childbearing to a later time in a woman's life. The number of births among

✉ Alicja Lachowska, e-mail: ala.lachowska@gmail.com

women of an advanced maternal age is constantly increasing, especially in women over 40 years of age [1,2]. According to US reports from 2006–2007 to 2014–2015, over this timespan there was an 8% increase in the number of births for women aged 40–44 and 26% for women aged 45–54 [3]. It is common knowledge that, as a woman ages, her reproductive potential decreases. An advanced maternal age (AMA), defined as >35 years, is associated with an increased risk of maternal and perinatal complications, especially in women over 40 years of age [4]. For women over 35 years, the fertilized egg will be of lower quality and exhibit reduced developmental competence. Due to decreased tubal function and a delay in oocyte transportation, the risk of ectopic pregnancy is between 4 and 8 times greater [5]. Maternal age is also a risk factor for miscarriages in the first and second trimester of pregnancy. An advanced maternal age increases the risk of chromosomal abnormalities in the foetus, which is a consequence of abnormal separation of chromosomes during cell division [6]. The exponential increase in the risk of chromosomal abnormalities occurs between the ages of 35 and 40 [7]. An advanced maternal age is also associated with an increased risk of pregnancy abnormalities and adverse obstetric outcomes. The newborns of women aged >40 years have a higher risk of heart defects and oesophageal atresia, which is twice as high as in younger mothers [8]. There is an increase in the number of labour dystocia and the rate of intrapartum caesarean sections in AMA women [9].

In developed countries, where the problem of delayed procreation is more common, women have access to assisted reproductive techniques (ART), which enable them to have children as late as after the age of sixty, by offering oocyte donation programmes [10]. Moreover, following in vitro fertilization (IVF), access to prenatal diagnostics allows foetal chromosomal abnormalities to be detected in women of advanced age. However, access to various ART procedures, as well as the age limit for women, depends on the legal regulations of a given country.

The aim of the study was to analyze the results of in vitro fertilization in women of very advanced maternal age (≥42Y) using autologous oocytes or donor oocytes compared to women ≤35Y.

Material and methods

This was a retrospective study of women of very advanced maternal age (≥42Y), who underwent intracytoplasmic sperm injection (ICSI) in the KrakOvi Clinic in Kraków (Poland) between 2021 and 2024. The control group consisted of patients aged (≤35Y). The research was carried out in accordance with the guidelines of the local bioethics committee.

The patients were treated using either the long agonist protocol (n = 28) or short antagonist protocol (n = 92). The type of protocol used depended on the level of AMH (Anti-Mullerian hormone) and the overall risk of hyperstimulation.

Long agonist protocol started one week before the expected menses (cycle day 18–23), when patients received the GnRH agonist, triptorelin (Decapeptyl, Ferring Pharmaceuticals, 1 mg/d, sc). After successful pituitary downregulation (when the serum estradiol [E2] levels were <40 pg/mL), ovarian stimulation was commenced with a fixed daily dose of 150–300 IU recombinant follitropin alfa (rFSH, sc) with or without an additional 75–150 IU menotropin (hMG).

A GnRH antagonist Cetrorelix (Cetrotide, Merck Europe, 0.25 mg/d, sc or Ganirelix, Gedeon Richter 0.25 mg/d), was administered, commencing when the largest follicle reached a diameter of 14 mm rFSH/hMG was initiated on day 2–4 of the cycle.

The agonist and antagonist protocols were continued up to and including the day of human chorionic gonadotropin (hCG) administration, which was when the leading follicle reached a diameter of 18 mm or more and at least three follicles reached a diameter of 17 mm or more. rFSH was then stopped, and a single sc bolus of 10,000 IU hCG (Eutrig – Samarth Life Sciences) or 6,500 IU rhCG (Ovitrelle – Merck) was administered 36 h before the planned time of oocyte retrieval. When there was a risk of OHSS in an antagonist cycle, the trigger was a single sc bolus of triptorelin 2 mg, and a freeze-all policy was applied. All follicles 12 mm or larger were aspirated.

Oocyte-cumulus complexes (COCs) were identified using a stereoscopic microscope, then washed and after 3 h of incubation (approx. 3 h) the cumulus cells were removed using hyaluronidase (Gynemed, Germany) and mechanical pipetting. Only oocytes in metaphase II with a first polar body were used for further procedures. Intracytoplasmic sperm injection (ICSI) was performed following the standard technique. Embryos were cultured in SAGE® medium (Origio, Denmark) under an atmosphere of 6.0% CO_2, 5.0% O_2 and balance nitrogen at 37°C. Embryo development was assessed every day. The blastocysts were graded according to the Gardner scoring criteria [8]. Blastocysts PGT-A tested were biopsied 120–124 h after ICSI (day 5), using the same micromanipulator and microscope used for ICSI. The zona pellucida was perforated using an Octax® laser (Vitrolife, Sweden) for 250 µsec. The biopsied TE cells were washed with D-PBS and placed in 0.2 mL polymerase chain reaction (PCR) tubes for PGS referral to Igenomix Inc. (Spain) and analyzed using next-generation sequencing (NGS). Following the biopsy, blastocysts were incubated for 1.5 h in Sage®medium and then vitrified.

The blastocysts were vitrified using Kitazato® media and the Cryotop device (Kitazato, Japan) according to the manufacturer's protocol. They were warmed in Kitazato media for a minimum of 1.5 h before transfer and then placed in EmbryoGlue® medium (Vitrolife, Sweden) medium.

Clinical pregnancy was identified by the ultrasound confirmation of an intrauterine gestational sac after 8 weeks of gestation with visible foetal cardiac activity. Ongoing pregnancy was confirmed when over 12 weeks of gestation had passed with visible foetal cardiac activity.

Statistical analysis

Non-parametric data, such as differences in the percentage values between groups, were assessed using the chi-squared test. Parametric data were expressed as means±SD and compared by two-way ANOVA. Differences were considered significant when the P-value was ≤0.05. The statistical analysis was performed using PQStat 1.6.2 (PQStat Soft, Poznan, Poland).

Results

The study analyzed the results of in vitro fertilization in 75 patients with advanced maternal age (≥42Y) and 45 patients aged <35Y. In the group consisting of patients ≥ 42Y, 45 of them used autologous oocytes and 30 took advantage of the oocyte donation programme. The results of IVF in the study groups are presented in Table 1 and Figure 1. In the group consisting of AMA patients, the AMH level was significantly lower (0.56 ng/ml) than in younger patients (3.6 ng/ml), ($p < 0.001$), which corresponded to a significantly lower number of oocytes (1.6±0.4 vs. 12±4 oocytes/cycle), ($p < 0.001$). In patients using donor oocytes, a standard package of six oocytes was used for one cycle. In older patients after fertilization with autologous oocytes only 0.4±0.1 blastocysts/cycle were obtained compared to 1.9±0.7 when donor oocytes were used and 3.8±1.1 from younger women. Due to the risk of genetic defects associated with AMA in the study group with autologous oocytes, as many as 83% of blastocysts were PGT-A tested with PGT-A and only 26% of euploid blastocysts were obtained. For comparison, in the group consisting of younger patients, only 51% of blastocysts were PGT-A tested, and the euploid rate was 57%. A similar euploidy rate (54%) was obtained in the group of older patients using donor oocytes. Only seven cycles (15%) ended in embryo transfer in the AMA group with autologous oocytes compared to 70% in the AMA group with donor oocytes and 75% in the younger group. Furthermore, the implantation rate was significantly lower in the group consisting of older patients with autologous oocytes (28%) compared to the other groups (50%, 59%), ($p < 0.001$).

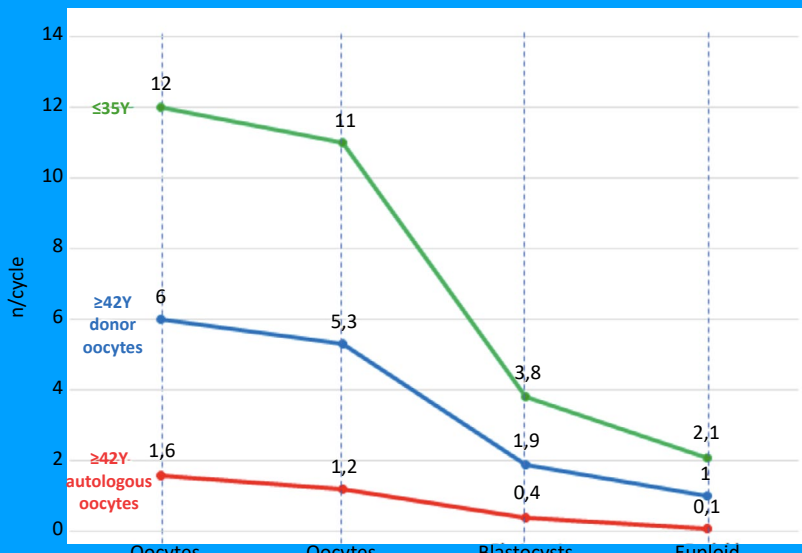
However, the number of ET (embryo transfer) in this group was so small that a large statistical error must be taken into account.

Table 1. In vitro fertilization results depending on women's age and type of oocytes (autologous or donor)

	Advanced maternal age		**Control**
	≥42Y autologous oocytes	**≥42Y donor oocytes**	**≤35Y autologous oocytes**
No. of patients (cycle), *n*	45	30	45
Age (years), range, mean±SD	42–50 43.5±1.5	42–49 43.7±1.6	28–35 32±2.8
BMI, mean±SD	23±2	23±3	22±2
AMH (ng/ml), mean±SD	0.56±0.3[a]	0.51±0.2[a]	3.6±0.8[c]
Oocytes recovery, *n* mean±SD	72 1.6±0.4[a]	-	540 12±4[c]
Oocytes M II, *n* mean±SD	54 1.2±0.1[a]	159 5.3±0.5[b]	495 11±2[c]
Blastocysts, *n* mean±SD	18 0.4±0.1[a]	57 1.9±0.7[b]	171 3.8±1.1[c]
PGT-A tested blastocysts, *n* (%)	15/18 (83%)[a]	24/57 (53%)[c]	88/171 (57%)[c]
Euploidy blastocysts, *n* (%)	4/15 (26%)[a]	13/24 (54%)[c]	50/88 (57%)[c]
ET (day 5) *n* (%)	3/45 (6%)[a]	10/30 (30%)[c]	16/45 (35%)[c]
FET, *n* (%)	4/45 (8%)[a]	11/30 (36%)[c]	18/45 (40%)[c]
Implantation rate, *n* (%)	2/7 (28%)[a]	11/22 (50%)[c]	20/34 (59%)[c]
Cycle cancelled due to lack of oocytes or blastocysts	21/45 (46%)[a]	7/30 (23%)[c]	6/45 (13%)[c]

BMI – the body-mass index is the weight in kilograms divided by the square of the height in metres, AMH – Anti-Mullerian hormone, ET – embryo transfer, FET – frozen embryo transfer,
a:b – values with different superscripts within the same rows differ significantly ($p < 0.05$)
a:c, b:c – values with different superscripts within the same rows differ highly significantly ($p < 0.001$)

Figure 1. Efficiency of IVF depending on women's age and type of oocytes (autologous or donor)



Discussion

Postponing procreation is becoming an increasing problem in developed countries. The issue of maternal aging is contributing to the intensive development of ART, preimplantation genetic diagnosis (PGD) and oocyte donation programmes (ODP) [11].

A marker of ovarian reserve and thus the chances of natural conception is AMH, which decreases with age, and a low or extremely low ovarian reserve makes natural conception impossible [12]. In our study, in the group of women of advanced maternal age we observed drastically lower AMH levels compared to women ≤35Y. In AMA patients we obtained only an average of 1.6±0.4 oocytes after hormonal stimulation, compared 12±1.1 oocytes from younger patients. Therefore, it can be assumed that for these women IVF is the only chance of achieving pregnancy. In one in four AMA patients we failed to obtain an oocyte capable of fertilization. With such a small number of oocytes, a correspondingly small number of embryos at the blastocyst stage are obtained.

In AMA patients, the problem is not only the quantity but also the quality of oocytes, which age together with the patient, and the chromosomal

disorders that occur in them lead to genetic defects in embryos [13,14]. There is no doubt that maternal aging contributes to the increased rates of aneuploidy in embryos. Therefore, for AMA patients, preimplantation genetic testing (PGT-A) is recommended. Over the last decade, preimplantation genetic testing (PGT-A) has become a very important tool for the selection of healthy blastocysts for transfer [15]. In the group of older patients, the embryo transfer at day 5 is most often abandoned because the patients decide to undergo PGT-A, but the problem is the small number of blastocysts that can be tested for PGT-A. Another key problem is the euploidy rate, which decreases dramatically with age. The euploidy rate of blastocysts obtained after fertilization of the autologous oocytes of AMA patients was 26%, compared to 57% in the group consisting of young women.

In the group of AMA patients using donor oocytes, significantly better results were achieved than with autologous oocytes, but worse than in younger patients, even though the oocyte donors are of a similar age to the control group. The poorer results may be due to the fact that the donor oocytes were vitrified, which could have impaired their developmental competence. In addition, the donation programme used packages of six oocytes/cycle and in the group of young patients, an average of 11 oocytes were fertilized. However, the euploidy rate of blastocysts was similar after the donor oocytes and oocytes from the group of young patients had been fertilized

To sum up, patients of advanced age must be made aware that using the IVF procedure does not guarantee pregnancy and the birth of a healthy child. Moreover, AMA patients should be offered pre-implantation PGT-A diagnostics due to the high risk of chromosomal defects. These patients should also be informed about the much higher effectiveness of IVF using donor oocytes.

References

1. Tough SC, Newburn-Cook C, Johnston DW, Svenson LW, Rose S, et al. Delayed childbearing and its impact on population rate changes in lower birth weight, multiple birth, and preterm delivery. *Pediatrics*. 2002;109(3):399–403.
2. Martin JA, Hamilton BE, Osterman MJK. Births in the United States, 2017. *NCHS Data Brief*. 2018;(318):1–8.
3. Sheen J-J, Wright JD, Goffman D, Kern-Goldberger AR, Booker W, et al. Maternal age and risk for adverse outcomes. *Am J Obstet Gynecol*. 2018;219(4):390.e1–390.e15.

4. Zipori Y, Linder R, Khatib N, Weiner Z, Barzilay E. Advanced maternal age and perinatal outcome in twin pregnancies: a meta-analysis. *J Matern Fetal Neonatal Med*. 2020;33(18):3193–3199.
5. Farr SL, Schieve LA, Jamieson DJ. Pregnancy loss among pregnancies conceived through assisted reproductive technology, United States, 1999–2002. *Am J Epidemiol*. 2007;165(12):1380–1388.
6. Kolevzon A, Gross R, Reichenberg A. Prenatal and perinatal risk factors for autism: A review and integration of findings. *Arch Pediatr Adolesc Med*. 2007;161(4):326–333.
7. Savva GM, Walker K, Morris JK. The maternal age-specific live birth prevalence of trisomies 13 and 18 compared to trisomy 21 (Down syndrome). *Prenat Diagn*. 2010;30(1):57–64.
8. Gill SK, Broussard C, Devine O, Green RF, Rasmussen SA, et al. Association between maternal age and birth defects of unknown etiology: United States, 1997–2007. *Birt Defects Res A Clin Mol Teratol*. 2012;94(12):1010–1018.
9. Martin JA, Hamilton BE, Osterman MJK, Driscoll AK, Mathews TJ. Births: final data for 2015. *Natl Vital Stat Rep*. 2017;66(1):1.
10. Laskov I, Michaan N, Cohen A, Tsafrir Z, Maslovitz S, et al. Outcome of twin pregnancy in women ≥45 years old: a retrospective cohort study. *J Matern Fetal Neonatal Med*. 2013;26(7):669–672.
11. Mastenbroek S, de Wert G, Adashi EY. The Imperative of Responsible Innovation in Reproductive Medicine. *N Engl J Med*. 2021;385(22):2096–2100.
12. Russell N, Gilmore A, Roudebush WE. Clinical Utilities of Anti-Müllerian Hormone. *J Clin Med*. 2022;11(23):7209.
13. Wasielak-Politowska M, Kordowitzki P. Chromosome Segregation in the Oocyte: What Goes Wrong during Aging. *Int J Mol Sci*. 2022;23(5):2880, https://doi.org/10.3390/ijms23052880
14. Van der Reest J, Nardini Cecchino G, Haigis MC, Kordowitzki P. Mitochondria: Their relevance during oocyte ageing. *Ageing Res Rev*. 2021;70:101378.
15. Yang H, DeWan AT, Desai MM, Vermount SH. Preimplantation genetic testing for aneuploidy: challenges in clinical practice. *Human Genomics*. 2022;16(1):69.