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Review Article

Anaesthesia Section

Anaesthetic Approach in Intrauterine Foetal Surgery: A Narrative Review

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ABSTRACT

Intrauterine foetal Surgery (IFS) has evolved from an experimental approach to an established treatment for certain life-threatening or disabling foetal conditions. It has witnessed remarkable advances in survival as well as long-term results. This has been due to advancements in high-resolution prenatal imaging, improved operative techniques, and a deeper understanding of foetal physiology. Anaesthesia in these procedures poses numerous unique challenges. These challenges require the anaesthesiologist to balance the complex and often competing physiological demands of the mother and the fetus while working under conditions that are high-risk and time-critical. This review integrates current anaesthetic methods and highlights emerging indications, such as fetoscopic laser photocoagulation for Twin-to-Twin Transfusion Syndrome (TTTS), foetal endoscopic tracheal occlusion for Congenital Diaphragmatic Hernia (CDH), and open or fetoscopic myelomeningocele repair. It covers key aspects of maternal-foetal physiology, concentrated foetal analgesia, ethical considerations, advances in foetal monitoring, and the integration of newly emerging technologies such as closed-loop anaesthesia systems, machine learning, and simulation-based training. Procedure-specific anaesthetic challenges associated with fetoscopic and ex utero intrapartum treatment procedures are discussed, along with the principles of postoperative care and their impact on long-term outcomes. Finally, the review identifies current knowledge deficits and directions forward that can lead to the standardisation of practice, enhanced patient safety, and evidence-based research to inform safer and more efficient anaesthetic care for foetal surgery. By incorporating technology and interdisciplinary approaches, anaesthesiologists can further advance the art and science of caring for two patients simultaneously during such remarkable procedures.

Keywords: Anaesthesia, Pregnancy, Maternal safety, Neonatal outcomes

INTRODUCTION

The IFS, at one time an experimental frontier, has emerged as a well-accepted method of treating selected life-threatening or disabling foetal malformations and conditions prior to birth. Advances in high-resolution prenatal imaging, foetal physiology, and Minimally Invasive Surgical Techniques (MIST) have enabled this shift. Procedures such as foetal endoscopic tracheal occlusion for CDH, fetoscopic laser treatment for TTTS, and open or fetoscopic myelomeningocele repair have shown significant benefits in selected cases [1]. These procedures present intricate anaesthetic challenges. The anaesthetist has to look after two patients at the same time-mother and fetus-who have distinct physiological demands. Maternal safety, foetal health, uterine relaxation, and preterm labour risk all need to be weighed in a time-sensitive, high-risk environment. No optimal anaesthetic techniques for these sensitive operations are universally agreed upon, and profound heterogeneity persists among centres undertaking foetal surgery [2]. This narrative review synthesises existing anaesthetic practice in IFS, discusses innovations and new indications, and outlines future research priorities to improve maternal-foetal outcomes. This review explores current anaesthetic practices in IFS, highlighting advancements, challenges, and future research directions to optimise maternal and foetal outcomes.

Spectrum of Intrauterine Foetal Surgical Approaches

Foetal surgical procedures can be categorised into minimally invasive surgery, open mid-gestational surgery, and the Ex-Utero Intrapartum Treatment (EXIT) procedure. Minimally invasive surgery is usually done in early to mid-gestation and encompasses needle-guided and fetoscopic methods. Needle-assisted interventions include ultrasound-guided access for procedures like percutaneous umbilical blood sampling, balloon valvuloplasty for critical aortic stenosis, and radiofrequency ablation for selective foetal reduction. Fetoscopic procedures, performed percutaneously under ultrasound guidance, include procedures such as Fetoscopic Endoluminal Tracheal Occlusion (FETO) for CDH, laser photocoagulation for TTTS, shunt insertions, amniotic band release, and, in some centers, myelomeningocele repair. These techniques obviate the morbidity of uterine incision and potentially preserve vaginal delivery in subsequent pregnancies. Open foetal surgeries entail a hysterotomy under regional or general anaesthesia and are generally reserved for the mid-gestational cases. They include open repair of myelomeningocele, excision of large lesions like sacrococcygeal teratomas or congenital pulmonary airway malformations, and temporary tracheal occlusion for CDH. Open procedures, however, require delivery by caesarean section in the index and subsequent pregnancy, leading to an effort to develop fetoscopic alternatives where possible. The EXIT procedure is a hybrid method designed to preserve placental perfusion during airway procedures at birth. It is mainly reserved for fetuses with potentially obstructive airway lesions in which postnatal immediate ventilation would be jeopardised. The procedure involves delivery of the foetal head and chest under general anaesthesia while the rest of the body remains attached to placental perfusion, permitting airway establishment prior to clamping the cord. EXIT has also been used to facilitate transitions to extracorporeal membrane oxygenation when needed. Foetal surgical procedures offer key benefits, including reduced maternal morbidity, preservation of vaginal delivery in future pregnancies, and the ability to intervene early with minimally invasive techniques, leading to lower complication rates. Open surgeries remain crucial for more complex foetal conditions but require caesarean delivery in subsequent pregnancies [2,3].

From Diagnosis to Decision: Expanding Indications for Foetal Surgery

The indications for IFS continue to expand as prenatal diagnosis and surgical capabilities advance [Table/Fig-1]. Lower urinary tract

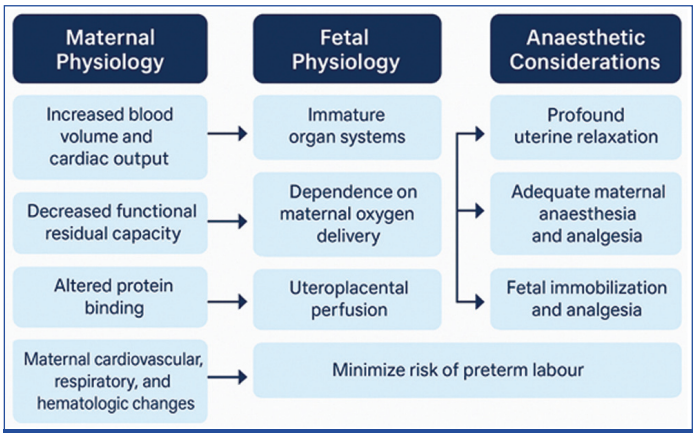
obstructions such as Posterior Urethral Valves (PUV) and severe hydronephrosis have historically been managed with vesicoamniotic shunting to relieve pressure and preserve renal function. Myelomeningocele repair before birth, as validated by randomised trials such as the MOMS study, has become a paradigm-shifting intervention. FETO has emerged as a promising option to promote lung growth in severe CDH [4,5]. Cardiac interventions aim to alter the course of evolving structural heart disease and prevent progression. Cervical teratomas or Congenital High Airway Obstruction Syndrome (CHAOS) require EXIT procedures to maintain foetal airway patency [6,7]. [Table/Fig1] summarises various intrauterine surgeries, their indications, and their outcomes [4-9].

Condition	Pathophysiology	Intervention	Goals/ outcomes
PUV, severe hydronephrosis [8]	Obstructed foetal urinary outflow causes oligohydramnios, renal damage, and pulmonary hypoplasia.	Vesicoamniotic shunting.	Decompress the urinary tract, preserve renal function.
TTTS [9]	Unequal sharing of blood between monochorionic twins. The recipient twin has heart failure and hydramnios, while the donor has anemia. It can be fatal to both.	Fetoscopic laser ablation of placental vessels.	Improve survival and reduce neurological morbidity.
Myelomeningocele [5]	Failure of fusion of the caudal neural tube causes neurological deficits, depending on the level of the lesion. The majority (80%) develop hydrocephalus. Deficit worsens progressively through gestation.	Prenatal open or fetoscopic repair.	Reduce the need for postnatal shunt, and improve lower limb motor outcomes.
CDH [4]	Diaphragmatic defect leading to herniation of abdominal organs into the chest. Leads to pulmonary hypoplasia and pulmonary arterial hypertension.	FETO.	Promote lung growth and improve survival in severe cases.
Critical congenital heart defects [7]	Severe valve stenosis or structural heart disease causes impaired cardiac output, ventricular dysfunction, or atrial hypertension, potentially leading to hypoplastic chambers.	Foetal cardiac interventions (aortic valvuloplasty, atrial septoplasty).	Prevent disease progression and preserve biventricular physiology.
Cervical teratomas, CHAOS [6]	Upper airway obstruction prevents neonatal breathing at birth; lungs become overdistended with fluid, causing hydrops and polyhydramnios.	EXIT.	Secure the foetal airway while maintaining uteroplacental circulation.

[Table/Fig-1]: Expanding Indications for IFS [4-9].

Physiological Balancing and Anaesthetic Considerations in IFS

A clear understanding of maternal and foetal physiology is crucial for providing safe and effective anaesthesia during IFS. Pregnancy causes profound maternal cardiovascular, respiratory, and haematologic alterations that impact anaesthetic drug distribution, metabolism, and haemodynamic responses. Increased cardiac output and blood volume, reduced functional residual capacity, and changes in protein binding may influence both the mother's anaesthetic needs and the foetal transfer of anaesthetic agents. Similarly, crucial is the fetus's own physiology, which differs from that of the mature organism and reacts differently to anaesthetic insult and surgical stress. Foetal oxygenation depends entirely on maternal oxygen delivery and uteroplacental perfusion, which maternal hypotension, uterine contractions, or excessive uterine tone can compromise. Therefore, careful maintenance of maternal oxygenation, normocapnia, and adequate uterine relaxation is critical to prevent foetal hypoxia and acidosis. Anaesthetic goals include providing profound uterine relaxation for surgical access, adequate maternal anaesthesia and analgesia, foetal immobilisation, and minimising the risk of preterm labour. These often competing objectives require a balanced approach using volatile anaesthetics, intravenous agents, tocolytics, and sometimes direct foetal anaesthesia. Close communication between the anaesthesiology, obstetric, and surgical teams is crucial for managing these physiological complexities effectively. Understanding these physiological intricacies sets the stage for effective monitoring, a cornerstone of intraoperative safety in IFS [10,11]. [Table/Fig-2] illustrates the foetal and maternal physiology, along with their respective anaesthetic considerations.



[Table/Fig-2]: Maternal and foetal physiology and anaesthetic considerations [10,11].

From Monitoring to Machine Learning: The Evolution of Intraoperative Vigilance

Continuous monitoring of both maternal and foetal status during IFS is crucial for detecting early signs of compromise and guiding timely intervention. Standard maternal monitoring includes electrocardiography, non-invasive or invasive blood pressure measurement, pulse oximetry, end-tidal carbon dioxide monitoring, and temperature measurement. Monitoring of arterial blood gases or central venous pressure may be warranted in prolonged or high-risk cases. Foetal monitoring has made significant advancements with the introduction of real-time ultrasonography, Doppler flow studies, and foetal echocardiography. All these modalities provide the added benefits of monitoring foetal heart rate, rhythm, and cardiac function during the procedure. Invasive monitoring, such as direct foetal pulse oximetry or blood sampling, is technically demanding and not frequently used, but it can yield important information in specific circumstances [3]. Near-infrared spectroscopy and foetal magnetocardiography are emerging technologies that have the potential to enhance intraoperative foetal monitoring through real-time, non-invasive assessments of foetal oxygenation and cardiac function. In light of all these innovations, the inability to identify minor or abrupt alterations remains a limitation that underscores the need for skilled staff and a prompt response to foetal distress signals. Optimisation of foetal monitoring is a multidisciplinary process that brings together anaesthetic, obstetric, and surgical skills to ensure the safest possible management for both mother and fetus during sophisticated intrauterine interventions [2,12].

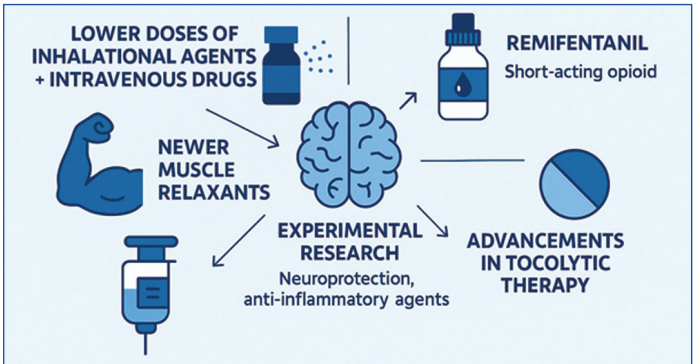
Targeted Foetal Analgesia and Ethical Considerations

The administration of effective foetal analgesia during intrauterine operations is a physiological and ethical requirement. There is evidence that the fetus can feel and react to painful stimuli by mid-pregnancy, as evidenced by hormonal, haemodynamic, and behavioural responses to invasive interventions. In the absence of effective analgesia and immobilisation, the fetus can undergo stress responses that may contribute to haemodynamic instability

and adverse neurodevelopmental outcomes [13-15]. In order to meet this, foetal analgesia is usually given in conjunction with maternal anaesthesia. Direct intramuscular or intravenous injection of opioid analgesics, muscle relaxants, and occasionally atropine is a usual approach given to the fetus prior to surgical maneuvering. This provides foetal immobility and obtunds stress responses with minimal excessive maternal sedation or uterine relaxation [16,17]. The ethical issue is focused on the obligation to treat the fetus not just as a surgical case but as an at-risk patient who is entitled to proper pain relief. This has to be weighed against maternal safety, since greater anaesthesia or more intense systemic agents risk adding to maternal danger. Informed consent, extensive counselling, and respect for parental autonomy are central to resolving these multifaceted ethical issues in foetal surgery programs [16,18].

Newly Emerging Anaesthetic Agents and Pharmacologic Trends

Continuing research on anaesthetic drugs and pharmacological techniques aims to enhance the safety and specificity of IFS [Table/Fig-3]. Conventional dependency on high levels of volatile anaesthetics for uterine relaxation may result in maternal hypotension, excessive bleeding, and delayed recovery. More recent techniques emphasise the optimisation of uterine relaxation and foetal anaesthesia by using reduced doses of inhalational drugs supported by brief-acting intravenous medications and newer tocolytics. Short-acting opioids such as remifentanil or fentanyl are more commonly utilised based on their extensive metabolism and advantageous transfer properties, making them ideal for precise titration for maternal and foetal requirements. Analogously, newer muscle relaxants with reliable pharmacokinetics facilitate safe foetal immobilisation with minimal maternal effect. Improvements in tocolytic therapy, such as agents like atosiban (an antagonist of oxytocin receptors) and newer beta-mimetics, provide improved uterine tone control with fewer systemic side-effects than older agents, including magnesium sulfate or terbutaline. Experimental studies are investigating the use of neuroprotective agents and anti-inflammatory drugs given perioperatively to prevent potential foetal cerebral injury related to surgical stress or anaesthetic exposure. While these developments are yet to be explored, they hold the potential to fine-tune anaesthesia regimens and enhance long-term care for both mother and infant [17-21]. [Table/Fig-3] depicts emerging agents for intrauterine anaesthesia.



[Table/Fig-3]: Emerging agents and experimental innovations [17-21].

Physiological Closed-loop Anaesthesia Systems in IFS

Physiological closed-loop anaesthesia systems represent an emerging frontier in the pursuit of safer and more precise anaesthetic management for complex procedures, including IFS. These systems utilise real-time physiological data- such as maternal depth of anaesthesia, haemodynamic parameters, and sometimes surrogate indicators of foetal well-being- to automatically adjust anaesthetic drug delivery within predefined safety limits. By continuously titrating anaesthetic depth based on patient-specific responses, closed-loop systems can maintain stable maternal haemodynamics, minimise fluctuations in uteroplacental blood flow, and reduce the risk of under- or over-anaesthesia. For foetal surgery, this stability is particularly beneficial because abrupt changes in maternal blood pressure or uterine tone can directly compromise foetal oxygenation. Although still primarily used in research or highly specialised centres, closed-loop technologies are being refined with advanced algorithms and machine learning capabilities. Future developments may integrate multi-parameter monitoring- combining maternal and foetal data- to create a truly adaptive system that supports both patients simultaneously. Such innovations have the potential to improve anaesthetic precision, enhance safety, and reduce the workload of providers during these technically demanding procedures [19,20].

Hybrid Operating Rooms and Real-time Imaging in IFS

The integration of hybrid operating rooms and advanced real-time imaging has greatly enhanced the safety and efficacy of IFS. A hybrid operating room combines the sterile environment of a traditional surgical theatre with high-end imaging modalities such as high-resolution ultrasound, fluoroscopy, and sometimes intraoperative magnetic resonance imaging. This allows multidisciplinary teams to perform complex interventions with immediate access to detailed anatomical and functional information. For anaesthesiologists, the hybrid setting is of utmost advantage. Real-time imaging on an ongoing basis enables accurate foetal positioning, correct placement of shunts or fetoscopic tools, and speedy identification of problems like bleeding, rupture of the membrane, or alteration in foetal status. Real-time imaging also makes administration of focused foetal anaesthesia safer and permits ongoing foetal heart rate and movement monitoring during crucial surgical phases. Hybrid operating rooms facilitate harmonious collaboration among obstetricians, paediatric surgeons, anaesthesiologists, and neonatologists, allowing for quick intraoperative adjustments. This arrangement is especially worthwhile for high-risk cases like the EXIT, wherein preserving the foetal airway with ongoing placental perfusion is a critical exercise requiring painstaking planning and immediate adjustment. With the development of technology, further centres are utilising hybrid operating environments, aware of their contributions to enhancing surgical accuracy, decreasing procedure time, and maternal and foetal safety in complicated intrauterine procedures [21,22].

Training for the Unexpected: Simulation in the Age of Foetal Surgery

Simulation and virtual reality have become revolutionary tools for educating anaesthesiologists participating in IFS. These high-fidelity training modalities enable practitioners to practice in challenging situations in a secure, controlled setting, maximising both technical skill and team coordination without risk to actual patients. Simulation training models the unusual but potentially fatal situations like sudden maternal hypotension, uterine rupture, unanticipated foetal distress, or those presenting during an ex utero intrapartum treatment EXIT procedure. Through crisis management training and developmental communication in anaesthesiology multidisciplinary simulations, anaesthesiology teams can become more responsive and confident in the operating suite. Virtual reality extends this even further by allowing for fully immersive and interactive simulations that emulate the specific challenges of foetal surgeries, including navigating constricted anatomical spaces, dealing with simultaneous maternal and foetal physiological alterations, and synchronising real-time imaging guidance. These resources also provide personalised scenarios that can be adjusted according to different skill levels, enabling ongoing learning and assessment of competency. Incorporating simulation and virtual reality into regular training, organisations can create highly competent and responsive teams capable of managing the challenges of contemporary foetal surgery programs, ultimately enhancing patient safety and outcomes [23-25].

Machine Learning and Workflow Optimisation

Machine learning and sophisticated data analysis are being increasingly investigated to refine anaesthesia care and workflow efficiency during IFS. These technologies review vast amounts of data from prior cases to identify patterns, predict risk, and provide evidence-based suggestions for anaesthesia management. Machine learning algorithms, in the case of foetal surgery, can assist anaesthesiologists in forecasting risks like maternal hypotension, hyperactivity of the uterus, or evidence of incipient foetal compromise by constantly analysing real-time physiological data. Predictive models can aid in more accurate drug titration, fluid administration, and the use of tocolytics, enabling proactive measures rather than reactive ones. In addition to providing intraoperative decision guidance, machine learning has the potential to optimise scheduling, resource planning, and team coordination in specialised foetal therapy units. Automated workflow systems can combine patient information, imaging data, and surgical planning to minimise delays and ensure that relevant expertise and equipment are readily available when needed. Although still in its early stages of clinical use, the application of artificial intelligence holds the potential to reduce variability in care, standardise complex protocols, and enable anaesthesiologists to provide safe, effective, and personalised anaesthesia for both mother and fetus. Ongoing research and validation will be essential to optimise the use of these tools in everyday practice [26,27].

Procedure-specific Challenges: Fetoscopic and EXIT Procedures

Each form of IFS involves special anaesthetic challenges that must be addressed with specific techniques to achieve the best results for mother and fetus. Fetoscopic surgery, like laser coagulation of TTTS or FETO in CDH, usually requires deep relaxation of the uterus in order to enable the precise handling of fragile foetal anatomy with the least trauma to the uterine wall. This frequently requires the administration of increased concentrations of volatile anaesthetics or other tocolytic drugs, which must be weighed against the risk of maternal hypotension and excessive bleeding. By contrast, the EXIT procedure is one of the most complicated situations in foetal surgery. EXIT is performed to secure the foetal airway or manage large cervical masses while maintaining uteroplacental circulation, thereby ensuring that oxygenation is not interrupted until the airway is secured. This requires deep general anaesthesia with maximum uterine relaxation to avoid contractions and premature placental separation, typically for an extended duration. Anaesthetic management thus needs to ensure stable maternal haemodynamics, adequate foetal paralysis and anaesthesia, and coordination with the obstetric and neonatal team, ready to resuscitate the neonate at the time of birth. Any compromise in uterine relaxation or maternal stability can lead to instant foetal hypoxia. EXIT procedure is one of the most technically and physiologically challenging interventions for anaesthesiologists [28-30]. [Table/Fig-4] shows a comparative table of the anaesthetic goals, drug choices, advantages, and risks for fetoscopic surgery and the EXIT procedure.

Postoperative Management and Long-term Outcomes

Postoperative care following IFS is a critical phase that directly influences maternal recovery, foetal survival, and the success of the surgical intervention. Maternal monitoring focuses on the early detection and management of complications such as haemorrhage, infection, pulmonary oedema from tocolytic use, or anaesthesia-related adverse effects. Continued uterine relaxation may be required postoperatively to prevent preterm labour, necessitating ongoing tocolytic therapy and close surveillance for signs of preterm contractions or membrane rupture. For the fetus, postoperative care involves serial ultrasounds to monitor growth, amniotic fluid volume, and the success of the surgical repair or intervention. Coordination with neonatology ensures that any residual or recurrent pathology can be addressed promptly at birth or in the neonatal period. Several factors, including the underlying condition, gestational age at delivery, surgical intervention, treatment success, and comorbidities, influence long-term outcomes. Repair of myelomeningocele, for instance, has shown better motor function and a lower requirement for ventriculoperitoneal shunting compared to postnatal repair, but it requires scrupulous neurodevelopmental follow-up [3,10,28,30].

Aspect	Anaesthetic goals	Common drug choices	Advantages	Risks
Fetoscopic Surgery (e.g., FETO, Laser Coagulation of TTTS) [28,30]	Deep uterine relaxation for precise foetal manipulation, minimal trauma to the uterine wall and foetal anatomy, stable maternal haemodynamics, and foetal oxygenation.	Volatile anaesthetics (e.g., Isoflurane, Sevoflurane), Tocolytics (e.g., Terbutaline, Magnesium Sulfate)	Effective uterine relaxation, minimal trauma to foetal anatomy.	Maternal hypotension, excessive bleeding, foetal bradycardia, and uterine over-relaxation.
EXIT Procedure [28,29]	Deep general anaesthesia with maximum uterine relaxation, secure foetal airway before clamping umbilical cord, maintain placental perfusion, and maternal stability.	General anaesthesia (e.g., Propofol, Isoflurane), Muscle relaxants (e.g., Rocuronium)	Maintains placental perfusion during surgery, secures foetal airway without interruption, and coordinates with the neonatal team for resuscitation.	Maternal hypotension, prolonged anaesthesia, risk of uterine rupture, and foetal hypoxia if poorly managed.

[Table/Fig-4]: Anaesthetic goals, advantages, and risks for intrauterine surgeries.

Current Gaps and Future Directions

Despite significant strides in foetal surgery and anaesthetic management, there are still major gaps that underscore the necessity of continued research and innovation. One of the significant challenges is the scarcity of globally accepted, evidence-based anaesthesia protocols for various forms of intrauterine interventions. There is variability in anaesthetic style, drug regimen, and standards of monitoring across centres, which tends to reflect institutional practice rather than consensus opinion. This heterogeneity has the potential to impact results and make multi-center collaboration and data comparisons challenging. The other essential gap is the paucity of information regarding the long-term neurodevelopmental effects of foetal anaesthetic exposure. More robust longitudinal studies are needed to clarify these effects and guide safer drug choices. Technological barriers also persist, including the need for more sophisticated, non-invasive foetal monitoring tools that can provide real-time feedback on foetal well-being during surgery. The integration of machine learning and closed-loop anaesthesia systems remains largely experimental and requires extensive validation before widespread adoption. Future directions should focus on multi-institutional collaborations to develop standardised protocols and registries for tracking maternal and foetal outcomes, as well as continued exploration of novel anaesthetic agents with improved safety profiles. Advances in simulation, virtual reality, and artificial intelligence promise to enhance training, planning, and real-time decision-making, paving the way for safer and more precise foetal interventions [31-33].

CONCLUSION(S)

The IFS has evolved from an experimental procedure to a life-changing option for select foetal conditions, improving survival and quality of life before birth. Anaesthesiologists face the challenge of maintaining the stability of both mother and fetus in a high-stakes environment. While advancements in surgical techniques and foetal

monitoring have improved safety, further research, standardised guidelines, and innovative solutions are needed. By embracing emerging technologies and refining strategies, anaesthesiologists will continue to play a pivotal role in shaping the future of foetal surgery.

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