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Fetal Intervention and Selective Reduction

Fetal intervention and fetal anesthesia provide clear opportunities for obstetricians and other professionals to evaluate and treat fetuses as patients. In pregnancies with multiple fetuses, there may be ethical conflicts that affect treatment options. Selective reduction of multiple gestations is an intentionally lethal action performed against one patient in order to benefit another. This is not morally different from abortion, regardless of any intended good consequences. Furthermore, there are many therapeutic options available to support a pregnancy with multiple gestations. Situations rarely arise where there is true maternal-fetal vital conflict due to a fetal condition, and ethical separation of the mother from the fetus may be indicated, but abortion itself is never medically necessary in these cases.

Background

Fetal Intervention

In maternal-fetal medicine, there are two patients involved in therapeutic relationship with the specialist. The fetus's status as a patient is perhaps most clearly seen when he or she needs medical or surgical intervention. In the past fifty years there has been significant growth in the field of fetal intervention. Since the time of early imprecise intrauterine transfusion using X-rays,[1] the field of fetal intervention has progressed to reducing morbidity in non-lethal fetal conditions, such as neural tube defects (NTD).[2] This bulletin provides an overview of fetal conditions for which treatment options are available, and to offer some additional guidance for related situations.

Fetal Conditions and Treatments

Twin-twin transfusion syndrome (TTTS) is a condition that complicates about 15% of monochorionic diamniotic (MCDA) twin gestations. It is caused by volume imbalance between two fetuses sharing a circulation through the anastomoses along the placental surface.[3] Left untreated, TTTS leads to mortality rates approaching 100%.[4] The gold standard of treatment for symptomatic stage I TTTS and stage II or higher TTTS is fetoscopic laser photocoagulation of the vascular anastomoses on the placental surface, which curtails the fluid imbalance by making the twins effectively dichorionic.

AAPLOG Practice Guideline. This document was developed by two authors on the Research Committee. Practice Guidelines are evidence-based documents informing pro-life providers with high-quality, peer-reviewed literature.

This also prevents consequences from monochorionicity such as the 25% risk of catastrophic neurological damage to a surviving cotwin, if one twin dies.[5] Other older, less effective treatments such as serial amnioreduction or septostomy are no longer routinely recommended.[3] Risks of fetal intervention are preterm prelabor rupture of membranes (PPROM, 38%), loss of one or both fetuses (14% and 9% respectively), and post-procedure recurrence of TTTS (11%) or twin anemia-polycythemia sequence (TAPS, 3%).[6,7] Selective reduction or abortion of the entire pregnancy is occasionally offered for TTTS, especially in stage III or higher. Abortion is never mandatory and is never the only option for maternal safety in TTTS, although previable delivery certainly may be.

Open neural tube defects (NTD) cause lifelong disability from a combination of anatomical defect and subsequent nerve damage from amniotic fluid exposure. Prenatal or fetal NTD repair decreases the length of time that nerves are exposed to amniotic fluid, and is the standard of care for some lesions.[3] In 2011, a landmark randomized controlled trial demonstrated that fetal repair outperforms postnatal repair for many fetal patients.[2] Fetuses with *myelomeningocele* (MMC) or *myeloschisis* should be evaluated in a fetal center and may be candidates for prenatal repair. Prenatal repair was classically carried out through a laparotomy and hysterotomy, but is now being performed fetoscopically and percutaneously in some centers.[8,9] Risks of open NTD repair include preterm delivery (66% between 30-36 weeks), PPROM (46%), labor (38%), and uterine incision dehiscence (10%).[2] Risks of fetoscopic repair result in longer intraoperative times, more PPROM (55% vs 46%), and more fetal skin dehiscence (20% vs 13%) compared to the MOMS trial, but offer similar gestational ages at delivery, similar rates of ventriculoperitoneal shunting, no risk of uterine rupture, and no requirement for Cesarean sections for all subsequent deliveries.[10]

Abortion is frequently offered upon diagnosis of NTD, especially for higher and longer lesions that are likely to result in severe disability. However, abortion represents an unnecessary lethal act on a fetus with a non-lethal, treatable condition. Some NTDs are not eligible for repair, and others are life-limiting in the neonatal period; perinatal palliative care is an optimal management strategy that avoids ending the life of the disabled fetal patient.

Congenital diaphragmatic hernia (CDH) leads to abdominal organs occupying the chest, leading to pulmonary hypoplasia. This can be lethal at birth if the neonate is unable to breathe from reduced functional lung volume and development. In *fetoscopic endotracheal occlusion* (FETO), fetal surgeons inflate a balloon in the fetal trachea, blocking it off and allowing buildup of lung secretions to inflate the lungs and push abdominal contents back into the abdomen.[11] This was recently shown to be beneficial for certain CDH patients,[12] but requires commitment from the family given the gravity of the intervention (the balloon is life-threatening

if the fetus is delivered). A fetal center should evaluate fetuses with CDH for eligibility for intervention, and whether the logistics of treatment are feasible for the family.

Abortion is at times offered for CDH especially with large lesions that are not eligible for FETO. In this setting, perinatal palliative care represents an option that does not cause the death of the fetal patient.

Abnormal fetal fluid collections, such as pleural effusions, megacystis, and pericardial effusions have long been targets of ultrasound-guided shunt placement in many centers. These shunts permit a return to normal physiology and fluid clearance. For example, a shunt may return fetal urine to the amniotic cavity to allow respiratory development, and decrease further injury to the kidneys.[13]

Finally, interstitial laser (utilizing a laser, directed at pathology inside the fetus) is occasionally used for vascular tissue-based applications, such as *sacrococcygeal teratomas* or *placental masses*.[14,15]

Abortion is extended as an option for families diagnosed with these conditions, since many of them portend life-long consequences (e.g. chronic kidney disease in LUTO). However, this represents a choice to end the life of a disabled fetus, rather than treat medically. Perinatal palliative care or fetal interventions represent other options in this setting.

Multiple other fetal interventions are currently under investigation, including serial amnioinfusions for renal agenesis,[16] ultrasound-guided fetal valvuloplasty,[17] laser photocoagulation of vasa previa,[18] and fetal repair of gastroschisis.[19] The field also anticipates significant noninvasive therapeutic advances in the next decades, with adult stem cell therapies and gene therapies showing promise in animal and adult trials.[20]

Fetal Anesthesia

Fetal surgery does not always require fetal anesthesia: for example, no anesthesia is required for laser photocoagulation of the placental surface. However, fetal pain control (e.g. opioids such as fentanyl) and paralytics (e.g. nondepolarizing agents such as vecuronium) are often given for procedures such as open NTD repair or FETO. This is required because fetuses experience surgical stimuli and react by moving away.

Fetal anesthesia is not routinely offered to fetuses undergoing selective reduction or dilation and evacuation (D&E), even if they are of similar maturity to fetuses who would require anesthesia to tolerate fetal surgery. These fetuses are able to sense the stimuli associated with dismemberment, as well as stimuli associated with arrhythmias or bradycardia, which have been shown to cause chest pain in pediatric patients.[21] Fetal pain is covered in detail in a separate guideline.[22]

Controlling Maternal Risk

Fetal intervention should be offered only if risk to the maternal patient is acceptably low. In cases of higher or uncertain

risk, interventions may be available under a research protocol at some centers.

It is the responsibility of the maternal patient's physician to ensure that she understands the risks and benefits of fetal intervention, both to herself and to her fetus(es). Even if maternal patients desire to accept very high personal risks on behalf of their fetuses, the pro-life OB/GYN retains a responsibility to equally care for and counsel the maternal patient as she is equally worthy of protection.

Selective Reduction

There are multiple approaches to counseling families with fetuses who are candidates for fetal intervention. One approach is to discuss risks and benefits to each person involved, including the maternal patient and each fetus. In a hypothetical case of stage II TTTS, perhaps the risk of laser photocoagulation is minimal to the maternal patient. In this example, laser would decrease the risk of death from 70% to 30% for the donor twin, and from 50% to 10% for the recipient twin, with low risks of fetal demise to both. There are also risks to the whole group of three patients, such as preterm prelabor rupture of membranes (PPROM), but these risks may be relatively simple for the family to weigh compared to the benefits.

At times, however, the life of one fetus seems pitted against the life of the other. In a hypothetical case of stage IV TTTS with a hydropic recipient twin and a difficult placental equator to access, the likelihood of death of the hydropic twin is very high and the risk of laser photocoagulation to the donor may be high as well. Because of the twins' shared circulation, expectant management is also high risk, since the death of the hydropic twin would rapidly cause hypotension in the co-twin, who hemorrhages into the low-pressure deceased twin. This can cause catastrophic, permanent neurological injury in the surviving twin, or may lead to a dual twin demise. In cases like this, it is tempting to view the pregnancy as a whole. With this utilitarian mindset, maximizing the chances of any good outcome (even one living baby) leads to treating the pregnancy *globally* rather than discussing each patient. The lowest-risk option to maximize the chance of one baby in this case is to perform selective reduction and end the life of the hydropic twin under controlled circumstances, before it can happen spontaneously. The effects of selective reduction appear the same as the best outcome of expectant management: a deceased recipient, and a neurologically intact donor.

These effects (or "ends") are good, but the action taken to obtain them (the "means") are not. Taking a global approach rather than a *patient-centered approach* leads to rationalization to abort, or selectively reduce, the sicker twin. Selective reduction represents an intentional, iatrogenic death of the sickest patient in order to help his or her twin. This procedure directly causes one of the disease's potential adverse outcomes, that is, fetal death, albeit in a controlled fashion,

rather than being an advocate for health of each patient.

Another common example of global risk reasoning being applied is when discordant anomaly (DA) is present in a set of twins: in this case, one twin has a major birth defect and the other does not. Twin gestations have risks of preterm birth (PTB), PPROM, and maternal pre-eclampsia, whereas after selective reduction, the maternal patient and the surviving fetus have risks equivalent to a singleton gestation. Given that one twin has a major anomaly and may die anyway, many providers and patients ask whether selective reduction should be used to lower the risk to the mother and healthy co-twin. The results for the anomalous twin will perhaps be the same, and the results for the mother and normal co-twin may improve. At first, selective reduction for DA appears to be the lesser of two evils.

Selective reduction here, however, is not a case of the lesser of two evils. It is true that the twin with the discordant anomaly has a disability and may not be expected to live long. It is also true that good effects may come about from the anomalous twin's death. However, neither the disability nor the "ends" of lowering risks justify a lethal act upon the anomalous, or disabled, fetus. Selective reduction in this case is equivalent to abortion for fetal anomaly in a singleton: it is discrimination against (and killing of) a disabled person. Rather than reduce or abort this disabled fetus, the pro-life physician must continue to care for him or her, as one among equals with his or her co-twin and mother.

Global risk reasoning is also commonly applied to multiple gestations, even without TTTS or anomaly. In a hypothetical case of quadruplets, the risk to the total pregnancy is increased by the sheer number of fetuses where any single fetus would fare better if there were fewer other living fetuses. The higher the number of fetuses, the greater the risk to each one. Again, a utilitarian approach justifies ending the life of one or more fetuses. But for a pro-life physician, reduction of the number of living persons by committing lethal acts is unacceptable. In this case as in others, selective reduction is morally equivalent to elective abortion even if there are potential good effects ("ends").

Advocating for All Patients

Regardless of the circumstances and the effects or "ends," selective reduction is categorically unacceptable to the pro-life physician because no ends justify the means of killing a patient. Other treatment modalities must be offered or utilized even if they may offer a globally higher risk, or a globally lower efficacy, to the group of patients.

The pro-life physician recognizes each patient, including the maternal patient and her fetus(es), as equally weighted in terms of the physician's duty to care.

Some patients' lives become difficult to protect because of illness; certainly there are times when the mother's life is in

imminent danger that requires separation from the fetus (see other Practice Bulletin). Other situations present difficulty in supporting each fetal life due to technical limitation (e.g., it may be difficult to perform TTTS screening in a set of monochorionic triplets when one triplet is difficult to visualize). However, the pro-life physician consistently respects the life and bodily integrity of each patient, regardless of the patient's contribution to the global risk.

Fetal Diagnosis

Genetic testing and ultrasound screening have become more sophisticated in the past thirty years. Non-invasive prenatal screening (NIPS, or non-invasive prenatal testing, NIPT) quantifies placental DNA in maternal serum as a way to screen for aneuploidy, and is being investigated for use in testing for fetal Rh status, microdeletions, and paternally-inherited monogenic disorders.[23] In addition, limited anatomy ultrasound is now available in the first trimester.[24]

There are pro-life providers who are averse to testing and communicating abnormal results out of concern that abnormal results make patients more likely to consider termination. These fears are founded in data that shows maternal patients with adverse fetal diagnoses are more likely to terminate pregnancy than the general population.[25,26]

Any form of pregnancy testing is, in itself, a neutral tool. Like all clinical tests, it should only be ordered if it will change management. Even if a patient would not choose *abortion*, results may still change the family's plans as they may prepare differently for the delivery of a child who may live a very short life, or a child who is likely to have disabilities. Preparation could include education, counseling, birth planning, support groups and subspecialty consultations.

The maternal patient should always be fully informed of her results regardless of the findings, and counseling should be detailed and specific about the anatomic or genetic finding and its relationship to her unique clinical variables. This provision of information is consistent with ethical traditions of honesty and integrity with information disclosure.

If the maternal patient does inquire about abortion after abnormal results are disclosed, it is the physician's right to act in accord with his or her conscience. Many prenatal care providers cannot suddenly move from caring for a fetus to supporting a decision to end his or her life. Such professionals are under no obligation to perform abortion or refer for abortion, since either course of action treats abortion as a therapeutic option. Even if a fetus is likely to die during the gestation or delivery, or shortly thereafter, anticipatory care is not equivalent to preemptively performing a lethal action.

Clinical Questions and Answers

Q *Must a maternal patient accept fetal therapy if it is available?*

All fetal therapy has risks to both fetus and mother, and the maternal patient is free to withhold her consent to fetal therapy for any reason even if intervention may be in the interest of her fetus.

This is because declining fetal intervention is based on the maternal patient's autonomy and the principle of informed consent. She must weigh the potential risks of the procedure for herself and the fetus(es) as compared with the potential chance of benefit. In so doing, she may reasonably decline interventions that involve undue burden or risks to her own body or deem that the benefits do not outweigh the risks to herself or the fetus(es).

This legitimate use of patient autonomy is different from the purported freedom to choose abortion, as this procedure affects not only her body but performs a lethal, rather than therapeutic, act upon the fetus's body.

Q *How should mirror syndrome associated with fetal hydrops be managed?*

Mirror syndrome is an urgent, life-threatening condition in which the maternal patient develops fluid overload symptoms (e.g. pulmonary edema) while carrying a hydropic fetus. Delivery is always and immediately indicated for mirror syndrome, even if the fetus is previable or anticipated to die.[27]

While the fetus may be expected to die from its condition or from prematurity, a physician should not hasten fetal death. Rather, a therapeutic approach to mirror syndrome restores health to the maternal-fetal dyad as much as possible, by separating them. Delivery can be performed by induction of labor or cesarean section, but must be pursued promptly while maternal medical care is provided. There is no need for dismemberment of a living fetal patient in order to treat maternal disease.

An indication to end pregnancy by urgent delivery is not the same as a "medical indication for abortion." Abortion is not medically necessary in these cases, as an urgent cesarean section can be performed in the case of acute threat to the maternal life. In this setting, a classical uterine incision is preferable to choosing dismemberment of a living fetus as a treatment for maternal illness.

Q *Is abortion indicated for untreatable, life-limiting fetal anomaly to protect the mother?*

A life-limiting prognosis in any patient is difficult, but in a pre-born child it can be particularly heartbreaking. Parents often immediately begin to grieve for the normal child they had anticipated, and grief can persist for many years, often recurring on the expected due date, the day of diagnosis, the delivery date, or the day of death. Given that grief begins at diagnosis and often persists for years, there is no role for abortion to curtail grief. There is no evidence that abortion improves the grieving process, although this has been widely taught

and is anecdotally reported. Instead, perinatal palliative care should be offered to address anticipatory grief and maximize the family's bonding with the brief life of their new family member.

Some cases of incurable life-limiting anomaly, such as anencephaly, are associated with maternal consequences, such as polyhydramnios, leading to shortness of breath and uncomfortable contractions. Delivery plans should be customized for each maternal-fetal dyad, but the ethical principle of proportionality can be followed (see Practice Guideline 10).[28] For example, if a woman carrying an anencephalic child is having difficulty breathing or sleeping in the early third trimester, an amnioreduction can be offered if she accepts the risks and benefits of this procedure. If she declines amnioreduction or if her symptoms persist despite amnioreductions, an induction of labor is reasonable despite the likelihood that the neonate will die slightly sooner given the preterm gestational age. It is neither necessary nor morally acceptable to dismember the fetus, administer chemicals such as potassium chloride, or induce labor prior to a proportion between maternal symptomology and the fetal condition, which can include early delivery to prevent fetal death so that the family can meet a living baby.[28]

In other cases, the morphology of the fetus may make vaginal delivery challenging, such as aqueductal stenosis or certain musculoskeletal dysplasias. In these cases, it is reasonable to plan preterm delivery for when the fetal head can still move through the pelvic outlet. In cases of hydrocephalus, another option is cephalocentesis prior to induction nearer term.[29] Ultrasound-guided cephalocentesis does have a low risk of fetal death, but if the maternal patient consents, it can be an ethically valid approach to achieving vaginal delivery. Within the framework of proportionality, the risk of fetal death is low, fetal death is not an intended outcome of the procedure, and the desired outcome is morally good (vaginal delivery to minimize maternal morbidity).

Q *Is treatment of twin reversed arterial perfusion sequence the same as selective reduction?*

Twin reversed arterial perfusion sequence (TRAP) begins as an MCDA twin set with discordant anomaly. Specifically, one twin has a severe cardiac abnormality which leads to anomalous body development, such as an absent or very small head, and an absent or very small upper extremities.[3] This condition results from poor blood flow from the abnormal heart of one twin, leading to acute or chronic brain injury, and underdevelopment of the upper body. It also ultimately results in lack of cardiac activity. After this fetus is effectively brain dead, the body (especially around the cord insertion, where oxygenated blood enters) continues to grow. This growth is solely because of blood flow created by the normal ("pump") twin through their shared placental circulation. Thus, even growth in size of the

deceased twin (called an "acardiac mass" in the literature) is not a sign of life.

The body of the deceased fetus, once it is no longer a living fetus, can be ethically separated from the living twin for the sake of optimizing the living twin's outcome. This is most often done by radiofrequency ablation, bipolar coagulation, or interstitial laser.

Summary of Recommendations and Conclusion

The following recommendations are based on good and consistent scientific evidence (Level A):

1. Fetal intervention is available for many anatomical defects identified during routine care of pregnancy.
2. Mirror syndrome represents a life-threatening maternal condition and delivery is indicated immediately even if the fetus will not survive.

The following recommendations are based on limited and inconsistent scientific evidence (Level B):

1. Results of detailed ultrasound and genetic screening should be made available to maternal patients promptly and accurately.
2. Perinatal palliative care can be offered in the setting of life-limiting anomaly.
3. Grief after life-limiting diagnosis begins at the time of diagnosis and often extends beyond the pregnancy.

The following recommendations are based primarily on consensus and expert opinion (Level C):

1. Abortion, that is, a lethal action performed on a fetus, is not indicated for any fetal anomaly as it does not medically benefit the maternal patient or the fetal patient.
2. Selective reduction is a lethal action against a patient and does not represent a true therapeutic option among fetal interventions.
3. Screening methodologies are morally neutral and should be ordered if they may change management, such as to support a family in preparing for a prenatal diagnosis.
4. Physicians are under no obligation to perform or refer for abortion.

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