Quality Norm on Invasive Fetal Therapy

(NVOG Kwaliteitsnorm Invasieve Foetale Therapie)

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Introduction

Invasive fetal therapy is nowadays an accepted form of specialized care for a small percentage of complicated pregnancies. The first procedure, intrauterine blood transfusion, was introduced in the 1960s, and has been considered established care already for decades. Later, other fetal diseases such as twin-twin transfusion syndrome have been shown to be treatable in utero. Invasive fetal treatment options have in common that they are technically challenging, associated with risks to the fetus including preterm rupture of membranes, preterm birth, fetal death and, although mostly limited, risks to the pregnant woman. The procedures require specific surgical skills, extensive training, specialized equipment and an experienced team, which is 24/7 available.

At least as complex is the diagnostic process, with careful patient selection, optimal timing of interventions, multidisciplinary assessment and counseling, specialized post-operative monitoring and planning of (timing, place and mode of) delivery. In The Netherlands, the current number of procedures performed is very low, in total less than 100 procedures per 100.0 births annually. Data from The Netherlands, all performed in one center, are shown in Table 1. Such limited numbers pose challenges to counseling, quality assessment, and teaching and training of new fetal surgeons.

With this Quality Norm on Invasive Fetal Therapy, the Dutch Society of Obstetrics & Gynecology (NVOG) aims to set a number of quality criteria, to ensure and good care for the individual pregnant woman who is confronted with potentially *in utero* treatable fetal anomalies in the Netherlands. Other aspects of specialized obstetric care, such as cost-effectiveness are not part of this quality norm.

Table 1. Invasive Fetal Therapy[1] in the Netherlands*

	Pregnancies			Procedures		
US guided needle procedures	**2012**	**2013**	**2014**	**2012**	**2013**	**2014**
Intrauterine blood transfusion						
Red Cell Alloimmunisation	24	17	14	71	41	37
Parvovirus B19, CMV	6	1	2	9	1	2
Other	8	4	9	17	6	16
Fetal Shunt procedures						
Hydrothorax, lung lesions	1	0	3	1	0	4
Lower Urinary Tract Obstruction	3	0	1	3	0	1
Total	**42**	**22**	**29**	**101**	**48**	**60**
Fetoscopic procedures						
Fetoscopic Laser for TTTS	56	55	64	57	56	66
Cord coagulation[2]	15	11	19	15	11	19
Total	**71**	**66**	**83**	**72**	**67**	**85**

1: Established procedures and indications, rare (<4/y), still experimental procedures not included.

2: Cord coagulation techniques used for selective reduction in monochorionic twins including twin reversed arterial perfusion sequence are: fetoscopic laser coagulation with or without transection, and US guided techniques including radiofrequency ablation, interstitial laser and bipolar forceps coagulation.

*data for Leiden University Medical Center

Requirements for an Invasive Fetal Therapy Centre (IFTC)

Requirements at a national level

1. Country-wide uniform inclusion and exclusion criteria.

2. Prospective collection of data of all fetal surgery procedures performed in The Netherlands (annual year report working party Prenatal Diagnosis and Fetal Therapy).

3. Website listing and explaining in lay terms the specific conditions managed and treatments offered in the field of Fetal Therapy.

Requirements for an IFTC

1. Availability of at least two doctors, sonographers and nursing staff with knowledge and experience in diagnosis, counselling and management in fetal surgery.
2. Access to consultation within 24 hours, 7 days per week.
3. Infrastructure, sterilised equipment and access to operating facilities within 24 hours at all times.
4. Full support for the fetal surgery program by the Department of Obstetrics and the Hospital Board of Directors.
5. Disease-specific protocols and Ethics Committee approval for all fetal surgery.
6. Protocols accessible not only to caregivers in the IFTC, but also to patients and referring physicians.
7. Regular multidisciplinary rounds with other specialists, including neonatologists, clinical geneticists, pediatric subspecialists (e.g. cardiology, nephrology, neurology, pediatric surgeons) and social workers, to discuss patients who may need or have undergone fetal interventions.
8. A setting and instruments for in vitro training.
9. An active program of research in the field of fetal therapy.
10. Prospective collection of data of all fetal surgery procedures performed in the IFTC (see for details Reporting and Monitoring paragraph).
11. Volume requirement: It is generally accepted that for complex surgical procedures, there is an association between experience, number of procedures performed per time unit, and outcome. In addition, to achieve an acceptable level of performance, novice surgeons require a period of training, during which they are gradually gaining competence, reaching expert level outcomes only after a certain number of procedures needed. For fetal surgery, recent publications on learning curves showed numbers to reach acceptable competence ranging from 20-61 procedures. Reliable figures on the number of fetal surgical procedures needed to maintain competence are lacking. In many fields of surgery for rare conditions, a minimum number of 20 procedures per year is mentioned, mostly without being validated by objective research data. In addition, there is debate whether such a number should be applied to each individual surgeon, or to an IFTC. Therefore, for this quality statement on requirements for an IFTC in The Netherlands, there appears to be insufficient data in the literature to demand a specific minimum number of procedures per IFTC and per specialist. For purposes of internal ongoing quality control (such as using CUSUM analysis), for maintaining team competence, and for the possibility of offering training to the few new surgeons needed over time, a careful analysis of the numbers of pregnancies requiring fetal surgery in The Netherlands, and from there, an assessment of the optimum number of fetal surgeons and IFTC’s seem desirable.

However, in the view of the total numbers the authors of this quality norm agreed that a reasonable minimum number per IFTC would be 20 interventions per year for each of the two main subcategories that are performed in the IFTC (needle guided therapy and endoscopic therapy). For innovative procedures and new IFTC's, a starting period of 3 years before achieving these numbers would be reasonable, with the prerequisite that at the start a plausible prognosis is provided that after the initial three years the required numbers are likely to be reached.

Requirements for the procedure

1. Continuous telephone access of the IFTC for the referring physician. Registration of the telephone consultations in the patient file (EPD). This applies as well for referral as for care after the fetal surgery.
2. Consultation includes ultrasonographic assessment, counseling and psycho-emotional guidance.
3. The IFTC should use up-to-date equipment and instruments for the specific type of fetal intervention.
4. Fetal surgeons are well informed on the changes in (back-up) equipment and instruments and the decisions of user committees that accompany the replacement or purchase of new equipment and instruments.
5. The protocol should address the possibility to turn to back-up equipment, should a defect occur before or during the operation.
6. All professionals involved attend the time-out and sign-out before and after the operation. Preoperative testing of the equipment should be part of the time-out.
7. The fetus should be monitored during the intervention.
8. In cases with postnatal viability, and after consent of the parents and neonatologists, a double setup must be described and guaranteed with the possibility of emergency cesarean section and a neonatal intensive care bed should be available.
9. Evaluation of the fetal status should be performed within 24 hours postoperatively. In cases with postnatal viability, postoperative fetal monitoring should be performed.
10. The fetal specialist monitors and is responsible for perioperative quality assurance.
11. High quality data registration is an integral and essential part of complex, low volume care, and serves many purposes, including reporting to the referring physician, ongoing assessment of safety and efficacy, separate reporting on incidents and complications, evaluation of technical improvements, and retrospective scientific research. The case manager is responsible for complete data input, as well as reporting and correspondence to the referring physician within 24 hours.
12. Before the patient leaves the IFTC, an evaluation interview should be performed and relevant feedback given to those concerned.
13. Once the patient is discharged and deemed stable, her longer-term postoperative and delivery care may be provided at another hospital. The most appropriate place will be advised case by case.
14. For each patient, a case manager should be appointed throughout the remainder of the pregnancy and the postpartum period.

Requirements for the fetal surgeon

1. It is expected that fetal surgeons will exhibit a learning curve as they begin to perform fetal invasive procedures. Ensuring that a level of expertise is achieved, requires a process of in vitro training and of intensive supervision by an experienced operator during the in vivo learning curve. The maintenance of an adequate level of expertise should be documented by ongoing reporting of the results of all procedures performed after the learning curve.
2. The portfolio includes performance on diagnostic and therapeutic procedures.
3. The portfolio includes proof that the operator can use the necessary equipment and also can solve common problems with the equipment.
4. The portfolio includes the attendance of specific courses (e.g. on the use of medical laser), international courses and meetings on invasive fetal therapy and internships in other IFTC's.

Requirements regarding Counseling

Aim of counseling

The ultimate aim of counseling is to help parents make well informed choices that are in the best interest of the mother as well as the child(ren).

<u>Requirements for the team (solely from the point of view counseling)</u>

1. The counseling team must at least include:
   - two, preferably three or more experienced physicians who are capable to discuss actual data on outcomes of different treatment options (see below).
   - a knowledgeable nurse or physician assistant to explain the procedure and answer questions.
   - a psychosocial worker to perform a psychosocial assessment of the family unit and guide women and their families in processing.
   - a clinical geneticist specialized in prenatal diagnosis.
2. The team should agree on the content of the counseling beforehand. Availability of a written counseling aid for the counselors and written information for the parents (example NICE guideline 180, see below) is recommended. These documents should be continuously updated as needed. The essential literature should be available for all parties involved. Counseling should be based on actual data from the literature and the IFTC itself.
3. Final counseling about treatment options should only be given after a full inventory of the fetal condition, including genetic testing if indicated, and a full assessment of maternal health and relevant chronic diseases.
4. If asked by the parents the team should be transparent about the experience of the individual physicians who are going to perform the procedure as well as about the institutional and team experience, and the annual volume.
5. The patient file should contain a detailed report of the counseling given
6. It is recommended to provide the patient with a copy of the correspondence about her case.

Requirements for the counseling proper

General issues

1. Realistic counseling should focus on chances on perinatal survival as well as on expected quality of life. This also means that on one hand the councilor should accept termination of pregnancy, and at the other hand refuses treatment, which is medically pointless.
2. Because of the high complexity of fetal surgery counseling should not only mention the most frequent complications but also the rare ones.
3. Because of the relative novelty of some forms of fetal surgery as a treatment option counseling should also address what is not known (e.g. long term outcome).
4. It should be clarified that results from experienced IFTC's may not be generalizable to interventions performed in other IFTC's.
5. Patients should be allowed to receive care at the IFTC of their choice and facilitated in organizing this.
6. Patients should also receive counseling as to the post-treatment period: signs and symptoms of complications, reasons to contact fetal therapy team, emergency alert symptoms.
7. Parents should be encouraged to consent to provide long-term follow up.

Contents of counseling

1. Discuss prenatally ascertained diagnosis and prognosis and eventual uncertainties.
2. Inform what would happen if condition was left untreated before birth (ie natural course of the disease if treatment is postponed till after birth (mortality and morbidity, outcome for the pregnancy as a whole and for individual infants if applicable).
3. Discuss options for management: expectant, termination of pregnancy if < 24 wks, various fetal surgical options, postnatal treatment, comfort care.
4. Explain selection criteria for the various treatment options and whether these apply for the patient who is being counseled.
5. Discuss advantages of fetal treatment in terms of mortality and morbidity for the pregnancy as a whole as for each individual infant if applicable.
6. Discuss short term risks/complications (frequency and nature) for the child(ren) with the different options : preterm birth including preterm birth at the border of viability, preterm rupture of membranes, chorioamnionitis, intrauterine demise, respiratory distress syndrome, low birth weight, intrauterine progress of damage if left untreated, difficulties during labour if left untreated.
7. Discuss local policies for management of children at the border of viability.
8. Discuss long term risks/complications (frequency and nature) for the child(ren) with the different options including neurological outcome.
9. Discuss maternal risks/complications (frequency and nature) with the different options: hemorrhage, need for transfusion, preterm delivery, preterm labour necessitating long-term admission, infection, placental abruption, amniotic fluid embolism, uterine scarring (hysterotomy), effect on future reproductive health.
10. Identify individual prognostic bad signs: short cervical length, obesity, history of vaginal bleeding, myomas, hypertension, placental position, history of preterm birth or miscarriages.
11. Finally weigh fetal benefit against maternal risk.
12. Ensure that the pregnant woman has sufficient time to take her decision.
13. Appoint psychosocial caregiver for support and aid in decision making. Aim to have this person present at medical consultations.

Requirements for new developments
The introduction of a new type of intervention should be preceded by an independent prospective risk evaluation. All departments involved, the local ethics committee and the board of directors of the hospital must agree with the decision to implement a new type of invasive fetal intervention. It is advisable that patient associations be involved with the prospective risk evaluation.

Long-term care

Long-term follow up is essential but complex due to the many variables that influence outcome. “On the fetal side” these factors are pregnancy- and birth-related as well as newborn treatment. “On the maternal side” complexity is due to the fact that the pregnant women may experience short or long term harmful side-effects. International collaboration and standardization should be encouraged when numbers are small.
In general it can be stated that a IFTC has a short- and long-term evaluation protocol containing fetal and neonatal / infant mortality and morbidity. Long-term results must be reported at least every five years in case of fetal therapy for structural anomalies.

Intrauterine transfusion
In The Netherlands intrauterine blood transfusion has been developed from an experimental therapy to established patient care. (1) Due to the invasive character with a (considerable) potential for fetal demise due to the procedure, close monitoring is obligatory.

Laser therapy for TTTS
Laser therapy for TTTS has developed from an experimental therapy to established patient care. Evaluation of the optimal technique and timing is on-going. Fetuses can die due to the procedure, and almost all infants are born prematurely. Maternal complications occur as well. Annual reports should contain information on numbers by TTTS stage, technique used, survival, gestational age at birth, short-term outcome and maternal complications. Reporting long-term outcome at least every five years can be expected to have an important additional value in terms of evaluation of the therapy.

Fetal surgical intervention in the presence of a congenital malformation (e.g. fetal aortic valvuloplasty, fetoscopic tracheal occlusion (FETO), bladder- and thorax-shunting).
Neonates and children should be cared for in (multidisciplinary) specialized clinics. This can be outside the IFTC as long as the resources are similar to those provided at the IFTC in order to maintain comparable care for ongoing outcome evaluation. A long-term evaluation protocol needs to be developed for each separate surgical intervention (and thus structural abnormality).

Reporting and Monitoring

An individual IFTC should report, at least on a yearly basis, on the total number of sessions, divided in subgroups (e.g. transfusion, balloon therapy, etc.). This is not only crucial for quality control and transparency, but also to improve counseling for future procedures. These reports need to be available for all groups involved, including (referring) specialists, pediatricians, boards of hospitals, insurance companies, and also to the public and have a standard format for the whole of the Netherlands.
Items needed per subgroup are:

- Definition of the (fetal) problem
- Procedure
- Gestational age at procedure
- Gestational age at birth
- Fetal / Neonatal outcome
    - Immediate
    - Follow up / Late
- Maternal outcome
    - Immediate
    - Follow up / Late
- Fetal Complications
    - Immediate
    - Follow up / Late
- Maternal Complications
    - Immediate
    - Follow up / Late

The reports will be used for a central Dutch registry, and data will also made available for international databases and comparisons with similar IFTC's in the world, with respect for the law regarding confidentiality and patient privacy.
IFTC's must be willing to review outcomes data and quality assurance. Peer review group(s), both national and international, will maintain an ongoing registry with an annual review process.

Fetal invasive therapy in The Netherlands

The fetus with a disease has become a patient and the general public has become familiar with the principles of diagnosis and therapy for the unborn. Apart from the needle-guided or fetoscopic procedures that today are routinely performed in the Netherlands (and that are listed in table 1) there are other forms of fetal therapy. Some of these therapies are non-invasive and thus not part of this guideline, others have been performed for a while but have later been abandoned, some are still experimental. For some indications (i.e. spina bifida and diaphragmatic hernia) Dutch patients are referred to Belgium. Especially the latter category has the potential to become part of invasive fetal therapy in the Netherlands in the future. The following list is itemized on disease, rather than on therapy:

- Thrombocytopenia has in the past been treated with weekly intrauterine transfusions of thrombocyte concentrations and is nowadays treated with maternal administration of IVIG.
- Cardiac arrhythmias are treated with maternal administration of antiarrhythmic medication (tachycardia) or adrenergics (bradycardia). However, in therapy resistant cases, intrauterine administration has been performed.
- Intrauterine growth reduction was treated fetal intravascular amino acid supplementation.
- Polyhydramnios of known or unknown origin is treated with amnioreduction.
- Premature prelabor rupture of membranes has been treated with intra-amniotic infusions, research on the effectiveness is ongoing.
- Congenital immunodeficiency has been treated with stem cell therapy.
- Hypoplastic left heart has been treated with balloon valvuloplasty.
- Fetal tumors are being treated with laser therapy (or RFA).
- Congenital diaphragmatic hernia (60 cases per year in the Netherlands) may lead to pulmonary hypoplasia. Fetal endoscopic (endoluminal) tracheal occlusion (FETO) has been shown to increase survival in severe cases. Fetoscopic insertion of a balloon (“plug” at 29 weeks) and removal (“unplug” at 34 weeks) is being performed.
- Fetal spina bifida (60 cases per year in the Netherlands) can be closedprenatally. This prenatal therapy is associated with better neurologic outcome, but also with higher rates of premature birth, than postnatal closure.

Referrals

In cases with suspicion of fetal anemia, hydrops, twin-to-twin transfusion syndrome, twin reversed arterial perfusion sequence, twin anemia polycythemia syndrome, the IFTC centre should be contacted immediately as referral and invasive therapy may be required within 24 hours. In cases with suspicion of diaphragmatic hernia or spina bifida or other congenital anomalies, referral (for specific diagnosis and counseling) should take place within one week. However, there is no reason for delay, so in those cases also, the IFTC should be contacted immediately.

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The quality norm should be reviewed no later than five years after the date.

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