Critical clinical situations in adult patients with Mucopolysaccharidosis (MPS)

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Abstract

Background: Mucopolysaccharidoses (MPS) are rare, inherited disorders associated with enzyme deficiencies that result in glycosaminoglycan (GAG) accumulation in multiple organ systems. Management of MPS is evolving as patients increasingly survive to adulthood and undergo multiple surgeries throughout their lives. As surgeries in these patients are considered to be high risk, this can result in a range of critical clinical situations in adult patients.

Results: We discuss strategies to prepare for and manage critical clinical situations in adult patients with MPS, including supporting the multidisciplinary team, preoperative and airway assessments, surgical preparations, and postoperative care. We also present eight critical clinical cases (age range: 21–38 years) from four leading inherited metabolic disease centres in Europe to highlight challenges and practical solutions to optimise the care of adult patients with MPS. Critical clinical situations included surgical procedures, pregnancy and a thrombus in a port-a-cath.

Conclusions: Individualised strategies to manage critical clinical situations need to be developed for each patient to compensate for the heterogeneous symptoms that may be present and the potential complications that may occur. These strategies should include input from the wider MDT, and be coordinated by metabolic specialists with expertise in the management of MPS disorders and surgery in adult patients with MPS.

Background

The mucopolysaccharidoses (MPS) are a group of rare metabolic disorders caused by deficiencies of lysosomal enzymes that degrade glycosaminoglycans (GAGs) (1). Across MPS subtypes and severities the majority of organ systems may be affected, resulting in a broad range of acute clinical situations requiring input from a range of specialities (2–4). Musculoskeletal, respiratory, cardiac, visual and auditory symptoms are common across all subtypes, while spinal cord compression and instability occur commonly in MPS I, II, IV and VI, and neurological problems occur in MPS I and severe MPS II, III and VII phenotypes (2–8). New diagnostic technologies and therapeutic developments have meant that patients increasingly survive into adulthood (9–12). The symptoms of MPS are progressive and are highly likely to require continued treatment throughout the patient's life. Although enzyme replacement therapies (ERTs) are available for the management of some symptoms in some MPS subtypes, and haematopoietic stem cell transplantation provides a further treatment option (9, 13–17), patients with MPS often require multiple surgeries throughout their lives to manage symptoms and support optimal quality of life (4, 18). Across the MPS subtypes, surgeries include, but are not limited to, cardiac valve replacement, spinal decompression, tonsillectomy, adenoidectomy, tracheostomy, hernia repair, corneal transplant and insertion of ventilation tubes (2–5, 18, 19). The combination of cardiac and respiratory dysfunction, spinal cord compression and instability, and anatomic abnormalities increases the risk of acute decompensation, requiring close surveillance pre-, peri- and post-surgery (4, 20, 21).

As patients with MPS reach adulthood, the responsibility for patient care is often transferred from paediatric to adult care teams, with the aim of allowing patients to become more independent and be more involved in treatment decisions if appropriate.(22) Although the transition process is a vital stage in supporting patients with MPS as they move towards increased independence, it is key to remember that patients have a progressive disease and the establishment of appropriate, individualised care plans in the adult setting is of great importance. Furthermore, an increasing number of patients with MPS are having children (23, 24). This may impose additional life-threatening situations during pregnancy and caesarean sections, which are required to compensate for short stature and skeletal abnormalities (24).

As MPS disorders have historically been considered paediatric diseases, the patient's adult care multidisciplinary team (MDT) may have less experience in managing the broad spectrum of potential critical clinical situations compared with paediatric colleagues. The continued involvement of paediatric specialists in the care of adults with MPS allows not only the provision of guidance and practical experience of the challenges of MPS, but also access to paediatric surgical equipment, which may be more suitable for adult MPS patients of small stature (4, 20, 22). Even within an adult metabolic setting, the rarity of MPS disorders and the high risk and low frequency of the surgical procedures in patients with MPS may limit opportunities for MDTs to gain practical experience of treating adults with MPS. Indeed, a survey of 1,900 anaesthetists found that only 34 of them had experience of adults with MPS (4).

The process of managing a critical clinical situation in MPS requires coordinated, expert input. This should be available from the point of determining if a particular procedure should go ahead, to carrying out a thorough preoperative assessment of the patient, to having a well-trained and prepared team available during the procedure, to understanding the potential complications and likely requirements of the patient during recovery. In this publication, we examine key factors that should be considered at each stage of managing a critical clinical situation in an adult patient with MPS, and examples of clinical strategies that could be used. We also present a series of cases involving critical clinical situations in adult patients with MPS, highlighting specific challenges that an adult care MDT may encounter and how these can be managed.

Results

Strategies to manage critical clinical situations in adults with MPS

Alongside collection of cases, healthcare professionals (HCPs) also provided key strategies that support the management of patients with MPS through critical clinical situations. These are summarised in Table 1.

Strategy	Details
Involve all relevant specialities in surgical preparations and incorporate into the MDT (Figure 1)	<p>Coordinate through a metabolic specialist</p> <p>Incorporate paediatric HCPs if additional expertise is required</p> <p>Ensure the MDT is provided with expert information on patient needs and possible complications</p>
Gain advice when developing standard operating procedures	<p>Collate input across the MDT</p> <p>Coordinate via a metabolic specialist</p> <p>Incorporate information from guidelines, recommendations, publications and congresses</p>
Monitor patient for progression of symptoms and development of adult-specific conditions (Multidisciplinary review and MPS Passport in Supplementary information)	<p>Monitor complex symptoms throughout the patient's life and new symptoms as they emerge</p> <p>Screen for common adult diseases, such as diabetes, cancer and hypertension</p>
Discuss surgical procedures with patient and family well in advance	<p>Allow patient and family to ask questions about surgery and choose where surgery is carried out</p> <p>Explain risks and benefits of proceeding with not proceeding with surgery</p> <p>Present other therapeutic options and likely outcomes</p>
Assess surgical risk (The preoperative assessment in Supplementary information)	<p>Collate information from the MDT</p> <p>Review pre-surgical assessment results</p> <p>Seek advice from paediatric anaesthetists on management of patients with MPS</p> <p>Balance risk of poor surgical outcomes with risk of no surgery</p> <p>Include input of patient and family preferences, and likely impact on quality of life</p>
Always carry out assessments prior to surgery (The preoperative assessment in Supplementary information)	<p>Coordinate pre-surgical assessments via the metabolic team</p> <p>Include:</p> <ul style="list-style-type: none"> • ECHO, ECG and pulmonary function tests • 3D CT of thorax and airways for any intervention involving general

	<p>anaesthesia</p> <ul style="list-style-type: none"> • Spinal and head MRIs and X-rays for spinal surgery • Laryngoscopy • Anaesthetic assessments <p>Carry out all assessments required for general anaesthesia, even if a local anaesthetic is planned</p> <p>Check availability of intensive care beds, potentially on paediatric wards</p> <p>Ensure imaging results are available during surgery</p>
Hold MDT meetings prior to surgery (The preoperative assessment in Supplementary information)	<p>Ensure appropriate surgical expertise is available</p> <ul style="list-style-type: none"> • Consider referring patient to an expert centre • Confirm surgical plans, and review current assessment results <p>Ask the following questions:</p> <ul style="list-style-type: none"> • Can the patient be ventilated with a mask? • What size equipment is needed? • How will positioning be managed during surgery? • Is the MDT ready for early extubation and tracheostomy? • Is the post-surgical team aware of any patient-specific requirements?
Stabilise symptoms prior to surgery	Manage cardiac and respiratory dysfunction that may increase surgical risk
Individualise procedures and equipment for each patient (Surgical preparations in Supplementary information)	<p>Review pre-surgery assessments</p> <p>Prepare paediatric equipment and replacement devices (e.g. cardiac valves) for patients of small stature</p> <p>Adapt post-surgical management (e.g. post-surgical fluid volumes) for patients of small stature</p>
Allow time for inclusion of additional procedures during surgery	<p>Make surgeons aware of the potential need to manage complications associated with scarring from previous surgeries and/or MPS pathology</p> <p>Be prepared for:</p> <ul style="list-style-type: none"> • Unsuccessful surgery • Problems with intubation

	<ul style="list-style-type: none"> • Haemorrhage • Post-surgical tracheostomy • Pain and/or discomfort • Infection
Anticipate need for emergency expert assistance during surgery	Ensure that paediatric anaesthetists, interventional radiologists and ENT specialists are aware of the procedure
Prepare a post-surgical care plan (Post-surgical care in Supplementary information)	<p>Ensure that different options are available based on surgical outcomes and emergency procedures</p> <p>Develop a rehabilitation schedule including a physiotherapist</p>
Support patient and family after the critical clinical situation	<p>Follow up patients with specialist members of the MDT</p> <p>Provide guidance on recovery and follow-up</p> <p>Ensure families support patients in following medical recommendations</p> <p>Provide prophylactic management and therapies to reduce negative impacts of ERT cessation</p>
Keep up to date with expert opinions	<p>Attend regional and national meetings</p> <p>Contact other experts for advice</p> <p>Incorporate recent guidance, recommendations and publications into standard operating procedures</p>

Table 1: Strategies for management of patients with MPS through critical clinical situations. CT, computed tomography; ECG, electrocardiogram; ECHO, echocardiogram; ENT, ear, nose and throat; ERT, enzyme replacement therapy; HCP, healthcare professional; MDT, multidisciplinary team; MPS, mucopolysaccharidosis, MRI, magnetic resonance imaging.

The preoperative assessment

The importance of a thorough preoperative assessment was highlighted as being key in bringing together the members of the MDT who will be involved in managing the critical clinical situation, ensuring that all necessary information is obtained and an expert opinion is provided. The preoperative assessment may be carried out as part of a multidisciplinary review at a one-stop clinic (Supplementary information: Multidisciplinary review and MPS Passport). The multidisciplinary review allows input from multiple disciplines, including metabolic specialists, cardiologists, anaesthetists, ear, nose and throat (ENT) surgeons, respiratory specialists, radiologists and physiotherapists (Figure). The outputs from this review are compiled into an MPS Passport, consisting of a clinical letter, images and videos, allowing any clinicians involved in the future management of a critical clinical situation, or clinicians located at

different sites, to gain a thorough understanding of individualised recommendations and any associated challenges. An example of the information that could be collected during the multidisciplinary review and entered in the MPS Passport is shown in the Supplementary information. This MPS Passport was developed by the Department of Anaesthetics at the Salford Royal NHS Foundation Trust, Salford, UK, and provides a reproducible, reliable approach for each patient. The multidisciplinary review is held as a single appointment, which is convenient for the patient and their carers, and also allows viewpoints from different specialities to be considered together. The images and videos can also be used to help patients and carers to understand the risks associated with any abnormalities of their airways or other investigation results.

As the standard tools and assessments used by anaesthetists may not be adequate for the assessment of patients with complex airways, such as those with MPS, a more thorough assessment involving an ENT consultant should also be carried out preoperatively (Supplementary information: Assessing the airways and preparing for emergency tracheostomy). Any challenges associated with previous surgeries should also be recorded. Assessing cardiac risk may be challenging because of reduced mobility, which means that tests which are used routinely in the general population, such as echocardiograms (ECHO) under stress, for example, are not always suitable for patients with MPS. Other suitable testing strategies may include transthoracic or transoesophageal ECHO, electrocardiogram (ECG), carotid intimal media thickness measurement and computed tomography (CT) coronary angiogram. In high-risk patients, and those expected to undergo long surgeries, intra-arterial blood pressure monitoring may be required.

The MDT must also prepare the family for any potential complications and negative surgical outcomes, such as an unsuccessful procedure and the risk of death during or after the procedure (Supplementary information: Discussing procedures with the patient and family).

Supporting the multidisciplinary team

If expertise in MPS is limited within a particular adult care setting, advice can be sought from metabolic paediatric colleagues. HCPs with specialist knowledge and experience in paediatric MPS, who are not core members of the adult MDT, are often involved in the preoperative assessment of adults with MPS and can provide guidance on or even undertake specific tasks. Furthermore, expertise may also be sought from external centres, and indeed HCPs with experience of surgery or anaesthesia in patients with MPS may travel to provide practical support during procedures, or virtual MDTs may be established to allow presurgical input from multiple external experts from centres in the same country or different countries. These adaptations to an internal MDT may be key if a second opinion is required or a patient with complex needs requires surgery. Although virtual MDTs do provide opportunities for geographically distant experts to be involved in key management decisions, this must be balanced with these experts having a less in-depth historical knowledge of the patient and the requirement for them to become familiar with the patient's presurgical assessment results. Patients may also be referred to an expert in a distant centre, but this may delay decision-making and can cause distress if patients need to travel long distances or be assessed by unfamiliar HCPs.

Specialised surgical equipment and surgical preparations

A full review of equipment and assessment results by the surgical team and an MPS expert prior to surgery will ensure that all requirements are in place (Supplementary information: Surgical preparations). Access to intraoperative monitoring options should also be investigated before surgery is performed. Motor evoked potential and somatosensory evoked potential measurements may both be used to assess the risk of ischaemia and paraplegia, and are key in managing surgical risk in MPS patients with complex spinal abnormalities, although these options may only be available in specialised spinal and neurosurgical units.

Patients with cochlear implants should not undergo procedures involving diathermy in the head and neck regions, although surgeons may not be aware of this (25), and it is key that all members of the surgical team should be informed of any factors that would require a divergence from standard surgical procedures.

Post-surgical plans

The recovery of the patient is also a complex, multidisciplinary process, which needs to be responsive to the outcome of surgery and any emergency procedures that were needed. Feeding plans need to adapt as the patient recovers, and individualised physiotherapy requirements should be in place to support the patient's rehabilitation (Supplementary information: Post-surgical care).

Cases

Critical clinical cases and their specific challenges are summarised here, with more details provided as supplementary information. These cases illustrate examples of the types of challenges that might be encountered during critical clinical situations in patients with MPS but should not be considered exhaustive.

Case 1 – Cardiac valve replacement

- Female patient with MPS VI, aged 34 years
- Aortic valve replacement
- Key team members:
 - Adult metabolic consultant, lysosomal storage disorder nurse, cardiologist, congenital heart disease specialist, cardiothoracic surgeon, paediatric and adult anaesthetist, ENT specialist, and respiratory consultant
- Surgery was conducted in a specialist cardiothoracic theatre by clinicians with expertise in congenital heart disease and previous experience in patients with MPS

- The team was prepared for risk of unsuccessful surgery, problems with intubation, bleeding, cardiac arrhythmias and post-surgical tracheostomy
- Recovery was considered to be 'good' in this patient, as her tracheostomy was removed after 8 days and she was able to walk with support 14 days post-surgical

Challenges and resolutions are presented in Table 2.

Table 2
Challenges and resolutions associated with surgery.

Challenges	Resolutions
Cardiac valve replacement	
<ul style="list-style-type: none"> • Initial intubation resulted in high CO₂ pressure • Nasal intubation via right nostril also resulted in high CO₂ pressure 	<ul style="list-style-type: none"> • Paediatric and adult anaesthetists with experience in MPS disorders present • Intubation via left nostril successful
<ul style="list-style-type: none"> • Patient's short neck made central line insertion difficult 	<ul style="list-style-type: none"> • Ultrasound-guided central line insertion by paediatric anaesthetist
<ul style="list-style-type: none"> • Pericardial adhesions from previous mitral valve replacement surgery at the age of 24 years • MPS-associated valvular pathology 	<ul style="list-style-type: none"> • Adhesions removed • Fibrous tissue, calcification and GAGs removed from mitral valve
<ul style="list-style-type: none"> • Physically small patient 	<ul style="list-style-type: none"> • Paediatric catheters used to remove excess blood from ventricles • Smallest adult replacement valve used (size 19 mm CarboMedics Top Hat® mechanical prosthesis)
<ul style="list-style-type: none"> • Tracheostomy required because of narrow trachea, but difficult for paediatric and adult anaesthetists to perform 	<ul style="list-style-type: none"> • ENT surgeon assisted • Pre-surgery 3D CT of chest and trachea, and fluoroscopy results were used to identify optimal site
<ul style="list-style-type: none"> • Spinal decompression 	
<ul style="list-style-type: none"> • No cardiology expertise in hospital performing surgery* 	<ul style="list-style-type: none"> • Medical files provided by the treating doctor • Surgeons discussed surgery with treating doctor to understand MPS-specific requirements
<ul style="list-style-type: none"> • Patient and family did not wish ERT to be interrupted by surgery* 	<ul style="list-style-type: none"> • ERT infusions arranged to occur during recovery at hospital performing surgery
<ul style="list-style-type: none"> • Patient had a short stature and restricted respiratory function[†] 	<ul style="list-style-type: none"> • Neurosurgeon had extensive experience in paediatric patients
<ul style="list-style-type: none"> • Corneal transplant 	
<ul style="list-style-type: none"> • High cardiovascular risk 	<ul style="list-style-type: none"> • Pre-surgery cardiac and respiratory function tests
<ul style="list-style-type: none"> • Risk that patient may not tolerate procedure or epithelium may be pierced 	<ul style="list-style-type: none"> • Make preparations in case general anaesthesia is required
<ul style="list-style-type: none"> • Risk of graft rejection 	<ul style="list-style-type: none"> • Endothelium preserved, resulting in reduced risk
*Case 2. †Case 3.	

Case 2 – Spinal decompression

- Female patient with MPS VI, aged 21 years
- Surgery to correct spinal stenosis and occipital spondyloses, involving installation of a halo device, laminectomy of the C1 vertebra, and resection of the foramen magnum
- Key team members:
 - Neurologist with experience of MPS, neurosurgeon, geneticist, cardiologist and anaesthetist
- Surgery was carried out at a hospital specialising in orthopaedics
- The patient recovered from the procedure without complications over a 2-week period in hospital with physiotherapy support

Measures to support the MDT are presented in Table 2.

Case 3 – Spinal decompression

- Female patient with MPS IVA, aged 21 years
- Surgery to correct spinal stenosis in the cervical region
- Key team members:
 - Metabolic specialist, orthopaedic surgeons, radiologist, neurosurgeons, anaesthetists and intensive care doctors
 - Surgery was carried out at a hospital specialising in orthopaedics
- The patient recovered from the procedure without complications but required physical rehabilitation during recovery because of muscular atrophy

Challenges associated with spinal decompression surgery are presented in Table 2.

Case 4 – Corneal transplant

- Male patient with MPS VI, aged 22 years
- Corneal transplant – deep anterior lamellar keratoplasty
- Key team members:
 - Adult metabolic consultant and nurses, ophthalmologist, adult specialist in corneal transplant, paediatric anaesthetist
- The team was prepared for pain, discomfort, infection and post-surgical haemorrhage
- Surgery was performed under local anaesthetic
- Recovery was as expected, and the patient could see shortly after the procedure

- He was discharged within 24 hours, and, along with his family, was advised on how to prevent infection and injury

Challenges associated with this case, and the steps put in place to mitigate these, are presented in Table 2.

Case 5 – Pregnancy

- Female patient with MPS I, aged 24 years
- Pregnancy, birth and infant care
- Key team members:
 - Obstetrician with expertise in inherited metabolic disorders, metabolic consultant, lysosomal storage disorder nurse, gynaecologist, midwife, general practitioner, cardiologist, genetic counsellor, anaesthetist and ophthalmologist
- Patient fell pregnant while ceasing to use contraception in preparation for corneal transplant
- Caesarean section planned for 38 weeks
- Baby born by uneventful spontaneous labour with epidural anaesthesia at 29+5 weeks
- The team was prepared to support the patient in caring for the infant as skeletal deformities and respiratory problems may have a negative impact on carrying the child and breastfeeding

Measures taken to support the patient during and after pregnancy are presented in Table 3.

Case 6 – Thrombus development in a venous access device

- Male patient with MPS II (Hunter syndrome), aged 26 years
- Thrombus in a port-a-cath and change of venous access device needed
- Key team members:
 - Metabolic consultant, lysosomal storage disorder nurse, infusion nurse, intravenous team, interventional radiologist, neurosurgeon, ENT consultant and anaesthetist
- Thrombus resolved using warfarin
- A Hickman line was inserted as a permanent solution for venous access
- The team was prepared for infections, further thrombi, blocked lines, and supporting the patient and family to manage the inconvenience of flushing access devices

Challenges of supporting continued ERT in this patient are presented in Table 3.

Challenges	Resolutions
Pregnancy	
<ul style="list-style-type: none"> Breathlessness and oedema progressed as ERT stopped at 3.5 weeks of the pregnancy 	<ul style="list-style-type: none"> Regular monthly obstetrics appointments Regular cardiology, ophthalmology and anaesthetic appointments Monthly fetal ultrasound scans
<ul style="list-style-type: none"> Spinal support required during pregnancy 	<ul style="list-style-type: none"> Body corset worn by patient
<ul style="list-style-type: none"> Neonatal child had squints, jaundice and respiratory difficulties 	<ul style="list-style-type: none"> Neonatal intensive care for 8 weeks Supportive ventilation
<ul style="list-style-type: none"> Help required caring for the baby for the first year because of joint restrictions in the hands 	<ul style="list-style-type: none"> Baby fed with expressed milk and formula Support provided by patient's family Increased frequency of health visitor appointments Appointments with occupational therapist
<ul style="list-style-type: none"> Chest infections more frequent and forced vital capacity reduced, as ERT cessation continued during breastfeeding 	<ul style="list-style-type: none"> Antibiotics prescribed once bacterial infection confirmed Contraindications confirmed with pharmacist
<ul style="list-style-type: none"> Maintaining ERT administration after thrombus development in a venous access device 	
<ul style="list-style-type: none"> Worsening breathlessness due to obstructive sleep apnoea 	<ul style="list-style-type: none"> Continuous positive airway pressure at night to resolve obstructive sleep apnoea prior to surgery to remove port-a-cath Assessed by neurosurgeon, ENT consultant and anaesthetist prior to surgery
<ul style="list-style-type: none"> After port-a-cath removal, patient received ERT by peripheral access, leading to reduced quality of life Port-a-caths are usually reserved for paediatric patients 	<ul style="list-style-type: none"> Hickman line inserted
<ul style="list-style-type: none"> Hickman line insertion resulted in patient distress 	<ul style="list-style-type: none"> Consider general anaesthesia for this procedure in patients with MPS
<ul style="list-style-type: none"> Risk of infection with Hickman line An adult Hickman line was required for an appropriate diameter, but as the patient is short, the line is relatively long, increasing infection risk 	<ul style="list-style-type: none"> Sterile dressings were changed frequently, and the line flushed prior to ERT Patient and family educated on managing Hickman line and infusions

<ul style="list-style-type: none"> • Patient travelling shortly after procedure 	<ul style="list-style-type: none"> • Sutures left in until patient was able to return
<ul style="list-style-type: none"> • Complex continuous symptom management 	
<ul style="list-style-type: none"> • Wide range of symptoms experienced, and surgeries and treatments required 	<ul style="list-style-type: none"> • Adult care specialist has extensive experience of MPS and makes personal contact with the MDT to explain the requirements for each surgical procedure • Continued monitoring of symptoms that are life-threatening or may affect quality of life
<ul style="list-style-type: none"> • Airway management during extubation* • Caused by swelling • Progressive dyspnoea developed after tracheostomy tube removal • Tracheal stenosis developed 	<ul style="list-style-type: none"> • Emergency tracheostomy • Oxygen support required on some occasions • Assess need for all future surgeries
<ul style="list-style-type: none"> • Surgical management[†] 	<ul style="list-style-type: none"> • Procedures can be carried out in a paediatric hospital that has appropriately sized equipment available and expertise in MPS
<ul style="list-style-type: none"> • Organisation of ERT infusions[†] 	<ul style="list-style-type: none"> • Carried out by adult care clinicians in a dialysis ward

Table 3: Challenges and resolutions associated with critical clinical situations.

*Case 7. [†]Case 8.

Case 7 – Complex continuous symptom management

- Male patient with MPS II (Hunter syndrome), aged 33 years
- Range of symptoms including respiratory, cardiac, neurological, gastrointestinal, skeletal, optic and dental
- Multiple surgical procedures throughout the patient's life to manage these, including adenoidectomy, tonsillectomy, T-tube insertion, inguinal and umbilical hernia repair, mastoidectomy, wrist surgery, dental surgery, hip replacement, tracheostomy, appendectomy, carpal tunnel decompression, two port-a-cath insertions, and a cardiac valve replacement
- Recurrent respiratory infections and otitis, hepatosplenomegaly, concentration difficulties, endocarditis, and craniocervical stenosis
- See Figure for key team members
- Because of previous issues regarding airway management during surgery, current skeletal symptoms are managed through pain relief and use of a wheelchair

Challenges in managing this patient are presented in Table 3.

Case 8 – Complex continuous symptom management

- Female patient with MPS I, aged 38 years
- Range of symptoms including motor delay, kyphosis, hip problems and pain, recurrent respiratory infections, otitis, diarrhoea, short stature, joint contractures, back pain, aortic valve insufficiency, craniocervical stenosis, severe visual loss, and loss of sensitivity in the first three fingers of both hands
- Cardiac valve replacement and spinal cord decompression surgeries
- See Figure for key team members
- Very narrow airways, so anaesthetic equipment included paediatric intubation tubes that would not have been available in an adult hospital

Practical steps to manage complex symptoms throughout the patient's life are presented in Table 3.

Discussion

This publication presents a range of challenges that may occur while managing critical clinical situations in adults with MPS. These challenges can be prepared for and resolved through practical steps and strategies, as outlined in Table 1 and the Supplementary information. Practical experience of managing critical clinical situations is often restricted to a limited number of specialist metabolic centres. Although some situations can be planned for in advance and the necessary expertise sought prior to the situation, for emergencies and time-limited procedures an awareness of MPS-specific requirements is needed to support HCPs in their treatment decisions.

In centres with experience of surgery in adults with MPS, there are opportunities to share this experience through providing advice and guidance, possibly through virtual MDTs, and training HCPs at other metabolic centres. It may even be an option for patients to undergo surgical procedures in these experienced centres, although this may limit the spread of knowledge if only clinicians from experienced centres are involved. Templates for preoperative assessments and post-surgical planning can be shared, and these may also assist less experienced centres in identifying areas in which increased experience is needed. Indeed, even experienced centres should seek to broaden their knowledge, as limited patient numbers mean that even an experienced centre may be managing small numbers of patients.

In adult metabolic centres with limited experience of MPS, the key is to seek out guidance from clinicians and centres that have carried out similar procedures and gain a full understanding of the challenges that are likely to be encountered. For example, difficult intubations because of narrowed airways are major factors in deferring complex surgeries (26). Theroux et al. examined potential abnormalities in patients with MPS IV, focusing on those that were specific to this patient group. Abnormalities of the airways

frequently result in difficult intubations in this patient group, not only because of GAG deposits in the airways but also spinal instability that affects the anaesthetist's ability to manipulate the patient's position. Intubation difficulties are estimated to occur in 25% of patients with MPS, so the MDT may wish to take additional steps prior to this procedure. This involves easy access to preoperative assessment results and imaging studies to guide the planned procedures, support for team members who are not familiar with the patient, and planned alternatives if initial procedures do not go ahead as expected.

Coordination of MPS care by a metabolic specialist ensures input from all relevant MDT members and that each patient's requirements are accounted for. This is particularly important for progressive heterogeneous diseases, such as MPS, where the types and severity of symptoms can vary widely between patients. The coordinating clinician should integrate information from across the wider MDT, ensuring that all relevant assessments are conducted, the results used to develop surgical plans and that the surgical team are aware of any potential complications. Patients with MPS are at high risk of surgical complications and knowledge of these is the key to optimising each procedure (4, 5, 20, 21). The metabolic specialist should also be involved in decision-making with regard to the potential benefits and risks of surgery. Thorough knowledge of the patient's condition and understanding of their past medical history and their social circumstances should be gathered prior to every procedure. While some patients may accept the risk of an additional post-surgical procedure, such as a tracheostomy, and are willing to undergo the procedure, others seem to develop tolerance to their stable and not troublesome symptoms and learn how to live with them. Because of the multi-organ involvement in MPS disorders and the potential for adverse impacts on surgery, where possible, symptoms should be resolved or stabilised before surgery is carried out.

Guidance on surgical procedures in MPS is already available, highlighting the importance of experienced team members and thorough preoperative planning (2–5, 21, 26, 27), and should be incorporated into standard operating procedures when possible. Charrow et al. have developed a series of consensus recommendations to support clinicians involved in any aspect of treating patients with MPS IVA (27). They again stress the need to carry out assessments with input from MPS experts, and to establish an MDT with a broad range of specialists to manage the needs of individual patients and provide a list of recommendations for anaesthetic and surgical preparations.

In terms of managing pregnant patients, many patients will undergo a planned Caesarean section. This may be because of either small maternal pelvis size or the position of the baby, but it is also important to consider the risk of a patient with MPS requiring an emergency general anaesthetic (24). Conversely, some patients might have increased intracranial pressure or hip dysplasia meaning that an epidural would be inappropriate. As with other surgery types in patients with MPS, recovery may be prolonged and a full preoperative assessment by an experienced MDT is needed. Plans should be in place for babies of mothers with MPS to be delivered in high-risk maternity units. Throughout pregnancy, some patients with MPS have been reported to experience pain, migraines, arrhythmia and blood pressure fluctuations (24), and plans should be in place to monitor and manage these.

The available literature exemplifies some of the guidance that is already in place to support the management of patients with MPS. A further important resource for metabolic specialists coordinating an MDT is national and international colleagues who are also responsible for metabolic patients. For rare disease HCPs, colleagues can offer information on different approaches to treatment, and alongside publications and case studies, this can deepen the expertise of the metabolic specialist. Conferences and meetings provide a further wealth of information across the field of MPS, which experts can use to inform up-to-date individualised care plans for each patient.

Conclusions

The progressive heterogenous nature of MPS means that every adult patient is different, and management of critical clinical situations in MPS is based on being constantly aware of the potential for these to occur and establishing an individualised MDT who are prepared to respond to such events. An MPS expert is key to ensuring that all members of the team are supported with the relevant knowledge, and strategies are individualised to the patient. As patients with MPS are increasingly living longer, they are increasingly managed by adult care teams instead of paediatricians. Strategies for MPS will continue to evolve as patients survive into adulthood and adult care teams gain further experience of managing these complex disorders. Current clinicians managing patients with MPS should be aware of the potentially large number of symptoms and complications to be considered, but also that guidance and expertise is available to support them in optimising treatment plans for their patients.

Methods

A group of experts including HCPs from centres with expertise in MPS from Germany, Spain, the Russian Federation and the UK met on two separate occasions to discuss transition management strategies for patients with MPS, and the management of adolescent and adult patients who have moved from paediatric to adult care. These centres all have experience of managing critical clinical situations in adults with MPS, and it was agreed that this expertise should be communicated to the healthcare community through a series of cases. These cases will provide examples of the types of factors that should be considered when preparing for interventions in patients with complex diseases, how paediatric specialists can be involved and how the wider MDT can prepare for potential challenges.

A series of teleconferences was organised to collect and discuss the required information and support publication development. Data and case studies were provided through written templates, telephone interviews and teleconferences between four contributing inherited metabolic disease centres in Europe:

- The Mark Holland Metabolic Unit, Salford Royal NHS Foundation Trust, Salford, United Kingdom
- Vall d'Hebron University Hospital, Barcelona, Spain
- HELIOS Dr. Horst Schmidt Kliniken Wiesbaden, Wiesbaden, Germany
- Research Center for Children's Health, Moscow, Russian Federation

The eight cases presented highlight a selection of procedures that might be carried out in patients with MPS and have been carried out according to current protocols.

Abbreviations

CT, computed tomography

ECG, electrocardiogram

ECHO, echocardiogram

ENT, Ear, nose and throat

ERT, enzyme replacement therapy

GAG, glycosaminoglycan

HCP, healthcare professional

MDT, multidisciplinary team

MPS, mucopolysaccharidosis

Declarations

Ethics approval and consent to participate: Not required

Consent for publication: Not applicable

Availability of data and materials: Not applicable as manuscript is based on case studies

Competing interests: CJH is owner and CEO of FYMCA Medical Ltd and Chief Medical Officer of and a shareholder in RareMD. CL has been a board member for BioMarin, Alexion, Shire and Genzyme; and received consultancy fees and grants from BioMarin and Shire, and payments for lectures from BioMarin, Alexion, Shire, Genzyme and Actelion. CL has also received travel, accommodation and meeting expenses from BioMarin, Alexion, Shire, Genzyme and Actelion. KMS has received travel grants from BioMarin, Genzyme, Alexion, Takeda and Chiesi, and attended advisory boards for Chesi and Takeda.

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Authors' contributions: KMS, AKG and GT have been involved in acquiring and interpreting data. CJH, TVL, JPL, MDT, NDV and CL were involved in the conception of the publication, and have been involved in acquiring and interpreting data. All authors have drafted or substantially revised the article, approved the submitted version and agreed to be personally accountable for their contributions and to ensure that

questions related to accuracy or integrity of any part of the work are appropriately investigated, resolved and documented in the literature.

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Critical care publication_supplementary information

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Supplementary information

Management strategies and case study details

Figures

Figure 1

Key members of the MDT for patients with MPS The MDT for patients with MPS consists of several HCPs . The main role of a tertiary adult metabolic centre is to coordinate the referral pathway to other specialists, arrange MDT meetings and follow up patients with MPS after procedures. In the UK model of care, a metabolic specialist coordinates referrals to other specialists and/or arranges preoperative assessments. Patients with MPS remain primarily under the care of a metabolic team, which works closely with the other specialists to provide the best possible care. The central coordinating position may

be filled by any specialty with the skills required to manage the patient's care plan among the other specialties involved.

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