orphanaesthesia

Anaesthesia recommendations for

Goodpasture syndrome

Disease name: Goodpasture syndrome

ICD 10: M31.0

Synonyms: Goodpasture's syndrome (GS), anti-glomerular basement membrane disease, crescentic glomerulonephritis type 1, GPS

Disease summary: Goodpasture syndrome is a rare and organ-specific autoimmune disease (Gell and Coombs classification type II). It is mediated by anti-glomerular basement membrane (anti-GBM) antibodies [7]. The disease was first described by Dr. Ernest Goodpasture in 1919 [6], whereby the glomerular basement membrane was first identified as antigen in 1950s. More than one decade later, researchers succeeded in defining the association between antibodies taken from diseased kidneys and nephritis [7].

The disorder is characterised by autoantibodies targeting at the NC1-domain of the α3 chain of type IV collagen in the glomerular and alveolar basement membrane with activation of the complement cascade among other things [7,17]. The exclusive location of this α3 subunit in basement membranes only in lung and kidney is responsible for the unique affection of these two organs in GPS [7].

Nevertheless, the aetiology and the triggering stimuli for anti-GBM production remain unknown. Due to the fact that patients with specific human leukocyte antigen (HLA) types are more susceptible, a genetic predisposition HLA-associated seems possible [4,7]. However, because this strongly associated allele is frequently present, there seem to be additional behavioural or environmental factors influencing immune response and disease expression. The latter may include respiratory infections (e.g., influenza A2), exposition to hydrocarbon fumes, organic solvents, metallic dust, tobacco smoke, certain drugs (i.e., rifampicin, allopurinol, cocaine), physical damage to basement membrane (e.g., lithotripsy or membranous glomerulonephritis) as well as lymphocyte-depletion therapy (such as alemtuzumab), but unequivocal evidence is lacking [4,7,9,17].

The incidence is estimated to be about 0.5 to 2 cases per million per year in European Caucasoid and Asian population [7,19,20]. Uncommon for autoimmune diseases, it affects more males than females in Caucasians, but it is even more common in the Maori people of New Zealand [19]. At once it is a cause of acute renal failure in approximately 10-20 % in all cases of rapidly progressive or crescentic glomerulonephritis. The age distribution shows two peaks. First between 20 and 30 years (with more frequent haemorrhagic features) and second between 60 and 70 years. Regarding the age pattern, the prevalence in the younger age group is higher for men whereas for women in the older age group [4,7].

GPS typically presents as acute renal failure caused by a rapidly progressive glomerulonephritis. This is often accompanied by pulmonary haemorrhage that may be life-threatening, especially without prompt diagnosis and treatment [7,17]. Symptoms may begin

slowly as well as a becoming rapidly progressive in a matter of days [1]. Fatigue, weakness, lethargy, nausea, vomiting, diarrhoea, pruritus, loss of appetite and weight, malaise, chills, fever, headache, arthralgias, a pale appearance and general discomfort or even seizures may be rather unspecific and initial symptoms [4,7,21,22,23]. About 60-80 % have clinically apparent renal and pulmonary manifestation, whereas 20-40 % have renal disease alone and in less than 10 % of the patients, manifestation is limited to the lungs [4,7,19]. Pulmonary symptoms include haemoptysis, dry cough, shortness of breath, inspiratory crackles over lung bases, chest pain, cyanosis, dyspnoea, tachypnoea up to respiratory failure [7]. Regarding children, they do not present commonly with pulmonary findings before puberty [15]. Affection of the kidney may lead to haematuria, foamy urine, swelling of the hands and feet, high blood pressure, oedema, uraemia, oliguria, anuria, and back pain in the kidney area [4,7,9]. Autoimmune inner ear disease (AIED) may be associated and presenting with vertigo, a ringing, hissing or roaring sound in the ear up to a sudden hearing loss in one ear progressing rapidly to the second ear (within weeks or months) [7].

More than 90 % of the patients with GPS have circulating serum anti-GBM antibodies [2]. A definitive diagnosis is substantiated by percutaneous kidney biopsy (preferred in comparison to a lung biopsy) and confirmed by immunofluorescent techniques and serum tested by enzyme-linked immunosorbent assay (ELISA) for the presence of pathognomonic circulating anti-GBM antibodies [7].

There is a lack of systematic data of this rare syndrome and no causal therapy or at least controlled therapeutic trials are available until now. Nevertheless, rapid recognition and treatment is crucial in GPS. The three principles in therapy of GPS are (1) to rapidly remove circulating antibodies (primarily by plasmapheresis), (2) to stop further production of antibodies using immunosuppression with medications (high-dose corticosteroids and cyclophosphamide represent the standard therapy, but other immunosuppressive agents like azathioprine or rituximab are also established), and (3) to remove offending agents that may have initiated the antibody production [7]. Renal-replacement therapy as well as renal transplantation may help to replace renal function. Most centres therefore recommend a 6 months period of sustained negative testing for anti-GBM antibodies before undertaking transplantation surgery [14]. There are several case reports of necessary extracorporeal membrane oxygenation (ECMO) due to refractory hypoxemic respiratory failure in GPS with severe pulmonary haemorrhage [1,3,9,12,15].

GPS has a poor prognosis, and it largely depends on timeline of diagnosis and treatment of this rapidly progressive disease. Untreated, the lethality of GPS ranges from 77–96% [9]. Under the triple therapeutic regime comprising corticosteroids, immunosuppressive therapy, and plasmapheresis, a survival of 70–90% in one year and up to 80 % in five years may be obtained [4,7]. Besides, in patients with dialysis due to end-stage renal disease in New Zealand and Australia, the median survival was nearly six years [20]. In addition to age, a history of pulmonary haemorrhage is associated with an increased risk of mortality on dialysis [12,20]. Dialysis dependency at presentation rarely generates full recovery of renal function. Nevertheless, patients requiring temporary dialysis may recover a good renal function and only less than 30 % of surviving patients require long-term dialysis [4,7,12,13]. Double positivity for serum ANCAs and anti-GBM is another indicative of a worse renal prognosis and higher mortality [4]. Pulmonal patients can also often fully recover from lung damage with fast and adequate treatment [3,19]. Long-term outcome in children with GPS might be better than in adults [15].

Medicine is in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

Emergency information

	AIRWAY / ANAESTHETIC TECHNIQUE	no special airway malformations, but GA may be challenging (due to respiratory status) – availability of tracheal suction (pulmonal bleeding) – anaesthesia only in cases of stable disease if applicable – be aware of severe / refractory hyoxaemic failure due to pulmonal haemorrhage with necessity of VV-ECMO – consider neuraxial / peripheral RA as a feasible alternative if applicable
B	**BLOOD PRODUCTS (COAGULATION)**	be prepared for recurring transfusions in case of persistent intrapulmonary bleeding (sufficient storage of blood products) – be aware of low platelets and fibrinogen in patients undergoing plasmapheresis
C	**CIRCULATION**	anticipate haemodynamic deviation due to pre-existing hypertension when undergoing anaesthesia – consider IBP (blood gas analysis) and (non-)invasive haemodynamic (to avoid fluid overload)
D	**DRUGS**	no risk for MH – be aware of secondary insufficiency of the adrenal glands (long-term corticosteroid-therapy) and infectious complications (immunosuppressive therapy) – consider drug dose adaption in case of renal impairment
E	**EQUIPMENT**	use ultrasound for vessel cannulation / peripheral RA (oedema, swollen limbs) – perioperative availability of dialysis may be necessary

Typical surgery

Percutaneous kidney biopsy and alternatively transbronchial or (rarely) open lung biopsy for diagnosis [7].

Bronchoscopy / (rarely) thoracoscopy for diagnostic issues [7].

Renal transplantation [7,11].

Arteriovenous fistula for dialysis.

Type of anaesthesia

A general recommendation regarding an ideal anaesthetic approach cannot be given, as there is a lack of data for anaesthesia in patients with GPS. As usual and whenever possible, anaesthesia should only be considered in cases of a stable disease.

Anaesthetists / intensive care physicians are often involved for securing the airway in instable GPS patients with pulmonary haemorrhage.

General anaesthesia might be challenging due to respiratory status of the patient with GPS.

Neuraxial (epidural) anaesthesia has been used in a patient with GPS undergoing bilateral nephrectomy, and it is described as uneventfully [16].

Peripheral regional anaesthesia techniques should be performable in most patients. Due to possible generalised oedemas, especially in the extremities, a landmark-guided approach may be difficult and ultrasound-guided regional anaesthesia is recommended.

Necessary additional pre-operative testing (beside standard care)

Chest radiograph: may show normal findings (18%) as well as infiltrates and patchy parenchymal consolidations, which are usually bilateral, symmetric perihilar and bibasilar [1,7,19].

Chest radiograph / ultrasound: pleural effusions are unusual but can occur [7,19].

Computed tomography: may reveal localised / nodular / diffuse / extensive / bilateral infiltrates with a pattern of alveolar damage [1].

Pulmonary function test: may help to better characterise or identify further progress of pulmonal impairment before scheduled surgery.

Blood testing: may show anaemia of variable degree (due to pulmonary bleeding or often secondary to iron deficiency as well as renal failure), high level of waste products as well as elevated blood urea nitrogen (BUN) and serum creatinine levels.

Urine analysis: proteinuria and / or haematuria may be observed.

Particular preparation for airway management

As far as known, there are no anatomic peculiarities due to GPS itself. Nevertheless, a standardized approach for airway examination and detection of airway challenges is recommended. A thorough preparation for airway management should be based on the examination results.

In case of pulmonary bleeding, urgent endotracheal intubation might be performed. Depending on the degree of haemoptysis and pulmonary bleeding in the individual patient, intubation performed via video-assistance or fibreoptic technique may be considered. Of course, direct laryngoscopy should be available too and for some anaesthetists and in individual (bleeding) situations this may be the more reliable option.

As the pulmonary bleeding usually is a bilateral phenomenon, lung separation techniques are normally not helpful for “separating a good from a bad lung”. In refractory bleeding with the development of severe hypoxemia, urgent transfer to an ECMO centre might be the only live-saving approach as a VV-ECMO might serve bridge-to-recovery in combination with the underlying medical therapy of the GPS.

Particular preparation for transfusion or administration of blood products

No specific recommendations are given. No typical bleeding disorders were reported for GPS patients. Nevertheless, problems may arise during plasmapheresis when platelets drop, and fibrinogen is removed.

However, patients with GPS often show significant anaemia (due to persistent intrapulmonary bleeding) with appropriate recurring transfusions [7,9]. Therefore, depending on scheduled surgery as well as the degree of haemoptysis/pulmonal bleeding, an adequate amount of blood products should be available.

Particular preparation for anticoagulation

Especially in cases of pulmonal haemorrhage, dialysis, or plasmapheresis the way and intensity of anticoagulation should be calculated by risk and benefit in each individual patient and depending on surgery.

Particular precautions for positioning, transportation and mobilisation

There are no specific recommendations for patients with GPS.

Interactions of chronic disease and anaesthesia medications

Long-term medication with corticosteroids should be considered due to secondary insufficiency of the adrenal glands. Thus, additional “stress dose corticosteroid dosing” might reduce the risk of perioperative adrenal insufficiency [24].

Immunosuppressive therapy might be related to a higher risk of infectious complications.

Anaesthetic procedure

Preoperative evaluation: see details above.

Premedication: might be performed weighing the benefits and risks in individual patients.

Patient positioning: no specific recommendations.

IV line: placement might be difficult due to swelling / oedema of the limbs [3,7].

Invasive blood pressure measurement: facilitates frequent arterial blood gas analysis, especially in case of pulmonal and renal (i.e. potassium levels) impairment.

(Mechanical) ventilation: pulmonary restriction and reduced diffusing capacity are characteristic in patients with GPS, moreover, ventilation should be performed lung-protective with adequate low tidal volumes to avoid baro-/volutrauma. Frequent tracheal suction due to pulmonal bleeding may be necessary [16].

Anaesthesia: total intravenous or balanced anaesthesia using volatile anaesthetics can be performed safely. The use of fentanyl, remifentanil and propofol is reported as uneventful for induction and maintenance [5,16]. An increased oxygen tension in anaesthetic gas mixture may be necessary due to pulmonal impairment, especially due to a pathologic degree of ventilation-perfusion [16]. There are no absolute or known relative contraindications for anaesthesia-related drugs just because of the disease GPS, but drug doses should be adapted depending on the degree of the patient's renal impairment. There is no specific risk for malignant hyperthermia.

Regional anaesthesia can be performed as described above.

Particular or additional monitoring

Haemodynamic monitoring (invasive or non-invasive): may be reasonable to avoid fluid overload in patients with GPS [7].

Possible complications

Pulmonal bleeding / haemorrhage and resulting respiratory failure / hypoxemia as well as anaemia.

Necessity of (long-term) dialysis due to renal failure.

Haemodynamic deviation due to pre-existing hypertension when undergoing anaesthesia.

Infections in case of fulminant immunosuppression.

Post-operative care

Post-operative care should be based upon the patient's pre-existing conditions as well as the surgical or interventional procedure.

Especially respiratory and renal function as well as blood pressure should be monitored in an appropriately extended stay in PACU, IMC or ICU before transfer to the normal ward (or discharge at home) is acceptable.

Disease-related acute problems and effect on anaesthesia and recovery

Emergency-like situations: diffuse alveolar or pulmonary haemorrhage with necessary ventilation, recurring re-intubations up to implantation of (VV-)ECMO in refractory hypoxemia due to pulmonary bleeding [3,7,19,21].

Differential diagnostics: Wegener granulomatosis, systemic lupus erythematosus, microscopic polyangiitis, other forms of systemic vasculitides (i.e., Churg-Strauss syndrome, essential mixed cryoglobulinaemia, Henoch-Schönlein purpura, microscopic polyarteritis, drug-induced vasculitis), pulmonary embolism, other disorders or infections (i.e., Pneumocystis carinii pneumoniae, rheumatoid arthritis) [4,7,19].

Ambulatory anaesthesia

Specific recommendations for or against ambulatory anaesthesia cannot be given as no published literature exists regarding this topic. In stable GPS disease, ambulatory procedures are possible if patients are ASA status I-III and do not show relevant contraindications for ambulatory anaesthesia.

Obstetrical anaesthesia

Patients with GPS are fertile, thus obstetrical anaesthetist might face women with GPS for labour analgesia. During pregnancy, the disease can seriously threaten the lives of both mother and child. Beside prematurity, abortion (on account of the teratogenic effect of an indispensable therapy) is possible. Gestational diabetes may occur due to steroid therapy. Therefore, an appropriate clinical management of pregnant women with GPS requires intensive care, a centre with an adequate expertise and a multidisciplinary co-operation among the attending medical specialists [8,10,22].

Hypertension and proteinuria are the most common findings in pregnancy in GPS. Although difficult during pregnancy, clarification whether this is caused by preeclampsia or renal abnormality due to GPS is important [10]. For definitive diagnosis, serologic studies and renal biopsy should be considered, whereby the latter one does not seem to be associated with an increased risk during pregnancy [22]. Beside blood pressure monitoring, the management of pregnant women with GPS should include a serial assessment of renal function, haematologic values and pulmonary function tests for assessment of a restrictive pattern or hypoxemia [23]. Deterioration in renal function may potentially exacerbate by pregnancy induced hypertension [22].

Vaginal delivery as well as caesarean section are reported in parturients with GPS [10,18,23].

In general, neuraxial as well as general anaesthesia might be performed in this patient population. Severe complications due to anaesthesia are not reported. However, the lack of reports on obstetrical anaesthesia should result in proper shared decision making regarding the selection of anaesthesia techniques for specific women.

References

1. Balke L, Both M, Arlt A, Rosenberg M, Bewig B. Severe Adult Respiratory Distress Syndrome from Goodpasture Syndrome. Am J Respir Crit Care Med 2015;191:228–229
2. Collard HR, Schwarz MI. Diffuse alveolar hemorrhage. Clinics Chest Med 2004;25:583–592
3. Dalabih A, Pietsch J, Jabs K, Hardison D, Bridges BC. Extracorporeal Membrane Oxygenation as a Platform for Recovery: A Case Report of a Child with Pulmonary Hemorrhage, Refractory Hypoxemic Respiratory Failure, and New Onset Goodpasture Syndrome. J Extra Corpor Technol 2012;44:75–77
4. Dammacco F, Battaglia S, Gesualdo L, Racanelli V. Goodpasture's disease: A report of ten cases and a review of the literature. Autoimmun Rev 2013;12:1101–1108
5. Fukuhara A, Okutani R, Oda Y. Anesthesia for living donor renal transplantation in a patient with Goodpasture's syndrome with a history of repeated alveolar hemorrhage. Masui 2013;62: 1199–1202
6. Goodpasture EW. The significance of certain pulmonary lesions in relation to the etiology of pneumonia. Am J Med Sci 1919;158,6:863–870
7. Greco A, Rizzo MI, De Virgilio A, Gallo A, Fusconi M, Pagliuca G, et al. Goodpasture's syndrome: a clinical update. Autoimmu Rev 2015;14:246–153
8. Hatfield T, Steiger R, Wing DA. Goodpasture's Disease in Pregnancy: Case Report and Review of the Literature. Am J Perinatol 2007;24:619–621
9. Herbert DG, Buscher H, Nair P. Prolonged venovenous extracorporeal membrane oxygenation without anticoagulation: a case of Goodpasture syndrome-related pulmonary haemorrhage. Crit Care Resusc 2014;16: 69–72
10. Huser M, Wagnerova K, Jnaju P, Malaskova L, Stourac P. Clinical Management of Pregnancy in Women with Goodpasture Syndrome. Gynecol Obstet Invest 2015;79:73–77
11. Lahmer T, Küchle C, Schirmer L, Heemann U, Lutz J, Thürmel K. Kidney Transplant After Preexisting Posterior Reversible Encephalopathy Syndrome Induced by Goodpasture's Syndrome. Exp Clin Transplant 2012;10:299–301
12. Levy JB, Turner AN, Rees AJ, Pusey CD. Long-Term Outcome of Anti-Glomerular Basement Membrane Antibody Disease Treated with Plasma Exchange and Immunosuppression. Ann Int Med 2001;134:1033–1042
13. Marques C, Carvelli J, Biard L, Faguer S, Provôt F, Matignon M, et al. Prognostic Factors in Anti-glomerular Basement Membrane Disease: A Multicenter Study of 119 Patients. Front Immunol 2019;10:1665
14. McAdoo SP, Pusey CD. Antiglomerular Basement Membrane Disease. Seminars in Respiratory and Crit Care Med 2018;39:494–503
15. Menzi CP, Bucher BS, Bianchetti MG, Ardissino G, Simonetti GD. Management and outcomes of childhood Goodpasture's disease. Pediatr Res 2018;83:813–817
16. Saegusa R, Ando M, Nishino T, Yonezawa T. Anesthetic management of bilateral nephrecto-my in Goodpasture's syndrome. The Japanese Journal of Anesthesiology 1977;26: 335–341
17. Salant DJ. Goodpasture's Disease - New Secrets Revealed. New Engl J Med 2010;363:388–391
18. Shah A, Bailey E, Hughes S. Goodpasture's syndrome, haemodialysis and pregnancy. Br J Hosp Med 2007;68:48–49
19. Sinha VK, Hibbert C. Near-lethal acute kidney injury due to Goodpasture's syndrome: A case report. J Intensive Care Soc 2015;16:350–354
20. Tang W, McDonald SP, Hawley CM, Badve SV, Boudville NC, Brown FG, et al. Anti-glomerular basement membrane antibody disease is an uncommon cause of end-stage renal disease. Kidney Int 2013;83:503–510
21. Ting IPL, Halim SA, Adnan A, Jaafar H. Status epilepticus as the initial presentation of antibody-negative Goodpasture's syndrome. BMJ Case Rep 2017:bcr-2017-219628. DOI: 10.1136/bcr-2017-219628
22. Vasiliou DM, Maxwell C, Shah P, Sermer M. Goodpasture Syndrome in a Pregnant Woman. Obstet Gyn 2005;106:1196–1199
23. Wells SR, Kuller JA, Thorp JM. Pregnancy in a patient with Goodpasture syndrome and renal transplantation. Am J Perinatol 1996;13:79–80
24. Woodcock T, Barker P, Daniel S, Fletcher S, Wass JAH, Tomlinson JW, et al. Guidelines for the management of glucocorticoids during the peri-operative period for the patients with adrenal insufficiency. Guidelines from the Association of Anaesthetists, the Royal College of Physicians and the Society for Endocrinology UK. Anaesthesia 2020;75:654–663.

Date last modified: **May 2021**

This recommendation was prepared by:

Authors

Christine Gaik, Anaesthesiologist, University-Clinic of Marburg; Germany
gaikc@med.uni-marburg.de

Thomas Wiesmann, Anaesthesiologist, University-Clinic of Marburg; Germany
wiesmann@med.uni-marburg.de

Disclosure The authors have no financial or other competing interest to disclose. This recommendation was unfunded.

This recommendation was reviewed by:

Reviewers

Martin Jöhr, Anaesthesiologist, Adligenswil, Switzerland
joehrmartin@bluewin.ch

Alan D. Salama, Nephrologist, UCL Department of Renal Medicine, Royal Free Hospital, London, Great Britain
a.salama@ucl.ac.uk

Disclosure The reviewers have no financial or other competing interest to disclose.