

Dąbrowska Izabela, Szydelko Joanna, Wolski Andrzej. Radiological diagnostics in patients with pheochromocytoma – do we need to prepare? Review of the literature. *Journal of Education, Health and Sport*. 2020;10(9):777-782. eISSN 2391-8306. DOI <http://dx.doi.org/10.12775/JEHS.2020.10.09.094>
<https://apcz.umk.pl/czasopisma/index.php/JEHS/article/view/JEHS.2020.10.09.094>
<https://zenodo.org/record/4052026>

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019.

© The Authors 2020;

This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland

Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike. (<http://creativecommons.org/licenses/by-nc-sa/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.

The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 22.09.2020. Revised: 24.09.2020. Accepted: 26.09.2020.

Radiological diagnostics in patients with pheochromocytoma – do we need to prepare? Review of the literature

Izabela Dąbrowska^{1a}, Joanna Szydelko^{2b}, Andrzej Wolski^{1c}

¹Department of Interventional Radiology and Neuroradiology, Medical University of Lublin, Poland

²Department of Endocrinology, Medical University of Lublin, Poland

^a nematoda@gmail.com, ORCID: <https://orcid.org/0000-0003-1593-2284>

^b jszydelko@interia.pl, ORCID ID: <https://orcid.org/0000-0003-3744-9058>

^candrzej.s.wolski@gmail.com, ORCID ID <https://orcid.org/0000-0002-2968-0949>

Corresponding author:

Izabela Dąbrowska

Department of Interventional Radiology and Neuroradiology

Jaczewskiego 8 Street

20-954 Lublin, Poland

phone: +48 81 724 41 54

e-mail: nematoda@gmail.com

Abstract:

Introduction: Pheochromocytomas are chromaffin cell tumours derived from the neural crest and they are associated with catecholamine production. Radiological procedures are playing essential role in present diagnostic of adrenal glands. Physicians who send their patients to the radiological examinations should prepare them to have a safe further diagnostic. A well radiologist should be aware of scanning protocols to provide best quality and the safest for the patient radiological examination.

Aim of the study: This article summarizes the current knowledge about radiological imaging of pheochromocytomas and scan procedures. In this paper we also want to answer to the question does a patient with pheochromocytoma need to be specially prepared for radiological procedures.

Description of knowledge: Diagnostic procedures play primary role in present diagnostic and treatment of pheochromocytomas. It is crucial for further diagnostic procedures to locate the tumour and its margins. Ultrasound imaging can be used with success only in big tumours with clinical symptoms. First choice for adrenal gland tumours is always CT. That modality easily shows localisation and tumours smaller than 1 cm. Another method of choice for adrenal imaging is MRI which gives high contrast images between soft tissues. Radiological differentiation of lesions wouldn't be possible without contrast agents. They are crucial for calculations of washout in CT.

Conclusions: Intravenous administration of non-ionic contrast agent for CT and gadolinium based in MRI is a safe practice for patients with pheos even without α -blocking medication. Only in an intra-arterial iodine-based contrast administration patient should be pharmacologically prepared before examination.

Key words: pheochromocytoma, adrenals glands, contrast agent, incidentalomas, radiology.

Radiological procedures play essential role in present diagnostic. Radiology is a useful tool for further diagnostic and treatment but also, we meet with many difficulties and rare situations such as uncommon syndromes or diseases. That situations require from doctors more work and quick review of their knowledge with the latest guidelines which are frequently changing during clinical practice. New technologies require different approaches and procedures. Nowadays we have fastest scanners, new scanning procedures, better quality of images and safer contrast agents.

In this paper we wanted to answer a question does a patient with pheochromocytoma need to be specially prepared for radiological procedures.

Pheochromocytomas (pheos) are chromaffin cell tumours derived from the neural crest and they are associated with catecholamine production¹.

Pheos are rare tumours, with an annual incidence of 2 to 9.1 per 1 million adults and may correspond up to 60% of all adrenal incidentalomas².

The majority of pheochromocytomas are benign but up to 25% of tumours may be malignant³. They affects equally males and females and they occur more frequently in the 3rd to 5th decade of life, but in literature there were cases of pheos in any age.^{3,4}

In children and younger patients, the disease is often hereditary⁵ up to 70% of cases⁶.

Rate of systolic and diastolic hypertensions is 0.2–0.6 in a group of patients with pheos^{7,8}. Pheochromocytomas may be an accidental finding (incidentalomas) or a a manifestation of hereditary syndromes⁹.

However 50% of these tumours remain undiagnosed because they are clinically silent during life – they were found post mortem¹⁰.

The primary treatment for a pheochromocytoma is still a surgery. This is why an adequate preoperative evaluation is crucial before surgery for patients^{11,12}. That evaluation should be very precise and include full patient's and it's family history, detailed blood tests, ECG and cardiac ultrasound.

All that preparations and pre-operative medical treatments are made to minimise intra-operative risk by blocking the effects of catecholamines for at least 10–14 days before surgery¹³ some authors recommend up to 21 days¹¹. Pharmacological treatment with α -blockade has been proven to reduce the number of perioperative complications to less than 3%¹⁴.

A β -adrenoceptor blocker may be used for preoperative control of tachyarrhythmias or angina. β -adrenoceptor blockers should never be employed without first blocking α -adrenoceptor mediated vasoconstriction¹³.

According to polish guidelines the treatment should last 10 - 14 days before surgery and first choice substance is phenoxybenzamine. First dose of phenoxybenzamine 10 mg p.o. 2 × day and slowly increase dose to maximum 1 mg/kg mc./day until achieve BP <140/90 mm Hg or

use doxazosin at first 2 mg p.o. in 1 dose or in 2 divided doses slowly increase the dose till max. 32 mg/day.¹³ In patients with high heart rate it's wise to add cardio selective β -blockers after blocking α -adrenoceptor. It is inadvisable to employ labetalol and carvedilol.

Volume contraction associated with chronic vasoconstriction can be seen in patients with pheos. That's why proper hydration is very important - pre-operative volume expansion achieved by saline infusion or increased water intake is recommended to reduce post-operative hypotension^{15,16}. Prophylaxis from vein thrombosis is mandatory¹⁷.

In the cases of inoperative and malignant pheos, the chronic medical treatment is the same as the preoperative treatment. The management of metastatic pheos remains palliative¹⁹. In cases that surgical resection is not possible, alternative include external beam radiation, cryoablation, radiofrequency ablation, transcatheter arterial embolization, chemotherapy, and radiopharmaceutical therapy¹.

New molecular targeted therapies that included everolimus, imatinib, sunitinib, had been used with various results¹⁸

Diagnostic procedures play primary role in present diagnostic and treatment. Radiological procedures like CT or MR show anatomical imaging and those images can be followed by nuclear functional imaging¹⁹. It is crucial to locate the tumour and its borders also infiltration to surrounding tissues¹⁹. Radiological imaging can be also a useful tool in diagnosing multiple primary tumours or metastatic lesions in patients with various genetic disorders²⁰.

Ultrasound imaging can be used only in tumours already measured in centimetres because small lesions could not be detected. On ultrasound, pheos have a variable appearance ranging from solid to mixed cystic and solid to cystic²¹.

Most used method of adrenal imaging is CT scan²². That modality easily shows localisation and tumours, size >1 cm in size with 87% to 100% sensitivity²³.

Pheos in CT imaging are often well-defined masses with attenuation values like those of muscle tissue, measuring approximately 30–40 HU²⁴ but it can be also less than 10 HU and the tumour may display more than 60% washout of contrast agents on delayed scanning. Proper diagnostic CT of adrenals demand administration of a contrast agent -pheos may have a higher absolute attenuation on the contrast phase and delayed scans allow to calculate the absolute and relative washout.

The adrenals can be also diagnosed in MRI. An MRI protocol for the adrenals should consist of both T1- and T2-weighted images²⁵. T1-weighted images obtained after intravenous administration of gadolin contrast agents are used to show enhancement patterns of adrenal lesions. In T2-weighted images we can notice a radiological sign called "light-bulb" because the tumour is bright and has a signal intensity of CSF²⁶. It is recommended to perform a MRI in large tumors prior to surgery to assess vascular invasion²⁷. MRI it is the safest choice for children and pregnant women because it doesn't use X-rays.

The main question is can we administer a contrast agent to a patient during CT or MRI after non-contrast-enhanced phase if we have a doubt, we have found an incidentaloma that could be a phoe? According to the latest ESUR Guidelines there is no need of special preparation for intravenous iodine- or gadolinium-based contrast agent in CT or MRI. Otherwise is recommended in examinations which require intra-arterial iodine-based contrast medium – in that case we have to orally administer drugs to block α and β -adrenergic receptors²⁸.

Bibliography:

1. Pacak K and Wimalawansa SJ: Pheochromocytoma and paraganglioma. *Endocr. Pract.* 2015.
2. Farrugia FA and charalampopoulos A: Pheochromocytoma. *Endocr. Regul.* 2019; **53**: 191–212.
3. Dahia PLM: Pheochromocytomas and Paragangliomas, Genetically Diverse and Minimalist, All at Once! *Cancer Cell* 2017.
4. Kiernan CM and Solórzano CC: Pheochromocytoma and Paraganglioma. Diagnosis, Genetics, and Treatment. *Surg. Oncol. Clin. N. Am.* 2016; **25**: 119–138. Available at: <http://dx.doi.org/10.1016/j.soc.2015.08.006>.
5. Pamporaki C, Hamplova B, Peitzsch M, et al: Characteristics of pediatric vs adult pheochromocytomas and paragangliomas. *J. Clin. Endocrinol. Metab.* 2017.
6. Landsberg L: Clinical features of pheochromocytoma and paraganglioma. In: *Contemporary Endocrinology*. 2018.
7. Manger WM: The protean manifestations of pheochromocytoma. *Horm. Metab. Res.* 2009.
8. Farrugia FA, Martikos G, Tzanetis P, et al: Pheochromocytoma, diagnosis and treatment: Review of the literature. *Endocr. Regul.* 2017; **51**: 168–181.
9. Gunawardane PTK and Grossman A: The clinical genetics of phaeochromocytoma and paraganglioma. *Arch. Endocrinol. Metab.* 2017.
10. Arnaldi G, Masini AM, Giacchetti C, et al: Adrenal incidentaloma. *Brazilian J. Med. Biol. Res.* 2000.
11. Pappachan JM, Raskauskiene D, Sriraman R, Edavalath M, Hanna FW. et al: Diagnosis and management of pheochromocytoma: A practical guide to clinicians. *Curr. Hypertens. Rep.* 2014.
12. Naranjo J, Dodd S and Martin YN: Perioperative Management of Pheochromocytoma. *J. Cardiothorac. Vasc. Anesth.* 2017; **31**: 1427–1439. Available at: <http://dx.doi.org/10.1053/j.jvca.2017.02.023>.
13. Bednarczuk.T, Bolanowski.M, Sworczak.K, et al: Adrenal incidentaloma in adults - Management recommendations by the Polish Society of Endocrinology. *Endokrynol. Pol.* 2016. Polish
14. Goldstein RE, O'Neill JA, Holcomb GW, et al: Clinical experience over 48 years with pheochromocytoma. In: *Annals of Surgery*. 1999.
15. Hack HA: The perioperative management of children with phaeochromocytoma. *Paediatr. Anaesth.* 2000.
16. Chen H, Sippel RS, O'Dorisio MS, Vinik AI, Lloyd RV, Pacak K: The north american neuroendocrine tumor society consensus guideline for the diagnosis and

- management of neuroendocrine tumors: Pheochromocytoma, paraganglioma, and medullary thyroid cancer. *Pancreas* 2010.
17. Gagner M, Pomp A, Todd Heniford B, et al: Laparoscopic adrenalectomy: Lessons learned from 100 consecutive procedures. *Ann. Surg.* 1997; **226**: 238–247.
 18. Baudin E: Treatment of malignant pheochromocytomas and paragangliomas. *Endocr. Abstr.* 2013.
 19. Shulkin BL, Ilias I, Sisson JC, et al: Current trends in functional imaging of pheochromocytomas and paragangliomas. *Ann. N. Y. Acad. Sci.* 2006; **1073**: 374–382.
 20. Ramachandran R and Rewari V: Current perioperative management of pheochromocytomas. *Indian J. Urol.* 2017.
 21. Bowerman RA, Silver TM, Jaffe MH, et al: Sonography of adrenal pheochromocytomas. *Am. J. Roentgenol.* 1981; **137**: 1227–1231.
 22. Lenders JWM, Duh QY, Eisenhofer G, et al: Pheochromocytoma and paraganglioma: An endocrine society clinical practice guideline. *J. Clin. Endocrinol. Metab.* 2014; **99**: 1915–1942.
 23. Varatorn R and Suchato C: Sabiston Textbook of Surgery The Biological Basis of Modern Surgical Practice 19th Edition 2012. *Bangkok Med. J.* 2012.
 24. Miyake H, Maeda H, Tashiro M, et al: CT of adrenal tumors: Frequency and clinical significance of low-attenuation lesions. *Am. J. Roentgenol.* 1989.
 25. Lee JK: *Computed Body Tomography with MRI correlation.*; 1998.
 26. Elsayes KM, Mukundan G, Narra VR, et al: Adrenal masses: MR imaging features with pathologic correlation. *Radiographics* 2004.
 27. Schteingart DE, Doherty GM, Gauger PG, et al: Management of patients with adrenal cancer: Recommendations of an international consensus conference. In: *Endocrine-Related Cancer.* 2005.
 28. Contrast Media Safety Committee: *ESUR Guidelines on Contrast Agents v10.0.* *Eur. Soc. Urogenit. Radiol.* 2018.