e-Reporting for Rare Conditions Secondary survey

Cushing's syndrome: the venous thromboembolism complications survey

1. Further information about this survey

Aim of this survey

To collect clinical data for the incidence of the VTE (venous thromboembolism) complications and for understanding the treatment processes and clinical outcome of cases with Cushing's syndrome (CS) of different origin that have been reported on the e-reporting platform (e-REC).

Governance

The EuRRECa project , includes e-REC which is approved by the UK research ethics service to collect non-personally identifiable clinical data and does not require individual patient consent, this includes the use of secondary surveys. However participating centres are advised to obtain local approvals at their own centre. The survey questionnaire utilises Webropol, a secure on-line tool that is endorsed and supported by NHS Greater Glasgow & Clyde and NHS Scotland. All information provided will be kept in compliance with the General Data Protection Regulation (GDPR 2016/679) and the UK Data Protection Act (2018). The EuRRECa project team will have access to the complete dataset and will provide data to research teams following approval by the Data Access Committee. These data will only be shared with investigators following the approval of the clinician who is responsible for the patient.

Further contact

It is possible that the EuRRECa project team may contact you again to check the data submitted and to provide you with further reports of the data.

The Registry team:

Prof Faisal Ahmed – EuRRECa project lead
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On behalf of the Endo-ERN Cushing and Thrombosis study group

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I confirm that I have read the above information and I am happy to proceed to the survey *

- ◯ Yes
- ◯ No

2. e-REC ID *

3. Clinician responsible for the patient (for any outputs from this work, this clinician will be contacted) *

4. E-mail address of clinician responsible for the patient *

5. Cushing's syndrome (CS) subtype

- ◯ Cushing’s disease
- ◯ Ectopic ACTH/CRH syndrome
- ◯ Benign adrenal CS
- ◯ Malignant adrenal CS

6. Age at presentation in years

7. Patient gender at presentation

- ◯ Male
- ◯ Female
- ◯ Trans

8. BMI at presentation

- ◯ Underweight (<20 kg/m2)
- ◯ Normal weight (20-24.9 kg/m2)
- ◯ Overweight (25-29.9 kg/m2)
- ◯ Obese (≥30 kg/m2)

9. Relevant co-morbidities at first surgery (select all that apply)

- ☐ Hypertension
- ☐ Obesity
- ☐ Diabetes mellitus
- ☐ Heart disease (e.g. myocardial infarction, myocarditis)
- ☐ Atrial fibrillation
- ☐ Cerebrovascular disease
- ☐ Stroke
- ☐ Venous thromboembolism
- ☐ Peripheral artery disease
- ☐ Chronic obstructive pulmonary disease (COPD)
- ☐ Asthma
- ☐ Chronic kidney disease
- ☐ Malignancy
- ☐ Osteoporosis with fractures
- ☐ Psychiatric symptoms
- ☐ Other, please speciify _____

10. CS severity index (total score)
(Please choose the appropriate score for each of the clinical features)

	0	1	2
Fat distribution: 0 = normal; 1 = mild truncal obesity with/without facies; 2 = marked truncal obesity with/without facies	◯	◯	◯

	0	1	2
Skin lesions: 0 = absent; 1 = mild manifestations of one or more of the following: striae and/or bruises and/or infections; 2 = severe manifestations of one or more of the following: striae and/or bruises and/or infections	◯	◯	◯
Muscle weakness: 0 = absent; 1 = mild (without functional impairment); 2 = severe (with functional impairment)	◯	◯	◯
Mood disorder: 0 = absent; 1 = mild (minor mood changes not requiring psychiatric help) 2 = severe (major mood disorder that substantially affects the individual levels of functioning and requires psychiatric help)	◯	◯	◯
Hypertension: 0 = absent (diastolic blood pressure ≤90 mm Hg) 1 = mild (diastolic blood pressure >90 and ≤105 mm Hg) 2 = severe (diastolic blood pressure >105 mm Hg)	◯	◯	◯
Diabetes: 0 = absent (decreased glucose tolerance may occur) 1 = mild (serum glucose <11 mmol/l) 2 = severe (serum glucose ≥11 mmol/l)	◯	◯	◯
Hypokalemia: 0 = absent (serum K >3.4 mmol/l) 1 = mild (serum K 3.4–3.2 mmol/l) 2 = severe (serum K <3.2 mmol/l)	◯	◯	◯
Sex-related disturbances: Female: 0 = absent 1 = mild manifestations of one or more of the following: hirsutism and/or hair loss; menstrual abnormalities 2 = severe manifestations of one or more of the following: hirsutism and/or hair loss; amenorrhea Male: 0 = absent 1 = decreased libido, occasional impotence 2 = impotence	◯	◯	◯

11. Medical treatment of CS before surgical treatment

- ☐ SRL 1st generation
- ☐ Pasireotide
- ☐ Dopamine antagonist
- ☐ Metyrapone
- ☐ Ketoconazole
- ☐ Levoketoconazole
- ☐ Mitotane

☐ Temozolomide

☐ Osilodrostat

☐ Not known

☐ None

☐ Other, please specify…. _____

12. If you have applied preoperative medical treatment (PMT), what was/were your goals of (PMT) in this patient with Cushing's syndrome? (multiple options possible)

☐ Decrease of cortisol excess

☐ Complete normalization of cortisol production

☐ Improved regulation of hypertension and/or diabetes mellitus

☐ Reduction of venous thromboembolism (VTE) risk

☐ Prevention of cortisol withdrawal syndrome

☐ Reduction of infectious complications

☐ Reduction of other surgery- related complications (e.g. bleeding)

☐ Reduction of psychopathology

☐ Other, namely: _____

13. When have you started PMT in this case?

◯ From diagnosis onwards

◯ X days pre-op (please, indicate) _____

◯ X days post-op (please, indicate) _____

◯ Other, namely: _____

14. When have you stoped PMT in this case?

◯ X days pre-op (please, indicate) _____

◯ X days post-op (please, indicate) _____

◯ Other, namely: _____

15. Cortisol excess status of the patient before surgery

- ◯ Uncontrolled CS (cortisol levels more or less unaltered)
- ◯ Partially controlled (significant and clinically relevant reduction)
- ◯ Controlled CS
- ◯ Other, namely: _____

16. Surgical approach to the patient

- ◯ Pituitary: Transsphenoidal approach
- ◯ Pituitary: Craniotomy
- ◯ Pituitary: Combined approach
- ◯ Adrenal: Laparotomy (open procedure)
- ◯ Adrenal: Laparoscopic/endoscopic procedure
- ◯ Other, namely: _____

17. Was it primary or re-do surgery?

- ◯ Primary
- ◯ Re-do
- ◯ Other, please specify _____

18. Does your center have a standardized thromboprophylaxis protocol?

- ◯ Yes, specific for CS
- ◯ Yes, but not specific for CS
- ◯ No

19. Did the patient receive thromboprophylaxis?

- ◯ Yes
- ◯ Yes, ongoing anticoagulant treatment for another indication

- ◯ No
- ◯ Not known

20. Thromboprophylaxis was prescribed by the:

- ◯ Endocrinologist
- ◯ Neurosurgeon
- ◯ Abdominal surgeon
- ◯ Haematologist or vascular medicine
- ◯ Anesthesiologist
- ◯ Other, please specify…. _____

21. The MAIN reason to start thromboprophylaxis BEFORE surgery in this case was:

- ◯ Obesity/overweight
- ◯ Severity of hypercortisolism
- ◯ Cardiovascular comorbidities
- ◯ Previous VTE
- ◯ Diabetes mellitus
- ◯ Limitation of mobility
- ◯ Non- 0 blood group
- ◯ Known hereditary thrombophilia (e.g. factor V Leiden/Prothrombin 2021a)
- ◯ Subtype of CS
- ◯ Current smoking
- ◯ Current oncology
- ◯ Older age
- ◯ All patients are started on thromboprophylaxis routinely
- ◯ Other, please specify…. _____

22. Thromboprophylaxis started BEFORE surgery, taking into account the following factors (multiple choices):

- [ ] No specific factors, all patients are started on thromboprophylaxis routinely
- [ ] Obesity/overweight
- [ ] Severity of hypercortisolism
- [ ] Cardiovascular comorbidities
- [ ] Previous VTE
- [ ] Diabetes mellitus
- [ ] Limitation of mobility
- [ ] Non- 0 blood type
- [ ] Known hereditary thrombophilia (e.g. factor V Leiden/Prothrombin 2021a)
- [ ] Subtype of CS
- [ ] Cushing's disease
- [ ] Ectopic ACTH/CRH syndrome
- [ ] Adrenal CS, benign
- [ ] Adrenal CS, malignant
- [ ] Current smoking
- [ ] Active cancer
- [ ] Older age
- [ ] Other, please specify…. _____

23. Thromboprophylaxis started:

- ◯ Before CS diagnosis (for other reason)
- ◯ From diagnosis of CS onwards
- ◯ One week pre-op
- ◯ 2 weeks pre-op
- ◯ 3 weeks pre-op
- ◯ The day before/of the surgery
- ◯ After surgery
- ◯ Other, please specify…. _____

24. Thromboprophylaxis started AFTER surgery, taking into account the following factors:

- [ ] Active disease (not in remission)
- [ ] Acute fall in cortisol levels (cortisol withdrawal syndrome)
- [ ] Severe immobilization
- [ ] Infection
- [ ] Known TE risks
- [ ] Other, namely: _____

25. Thromboprophylaxis stopped:

- ◯ One week post-op
- ◯ 2 weeks post-op
- ◯ 3 weeks post-op
- ◯ 4 weeks post-op
- ◯ 6 weeks post-op
- ◯ 12 weeks post-op
- ◯ Before surgery
- ◯ Other, please specify…. _____

26. Which medications for thromboprophylaxis were used:

- [ ] Low-molecular weight-heparin (LMWH)
- [ ] Direct oral anticoagulants (DOACs)
- [ ] Warfarin
- [ ] Aspirin
- [ ] Other, please specify…. _____

27. What LWMH has been used?

- [ ] Nadroparine
- [ ] Enoxaparin

- [ ] Dalteparin
- [ ] Ardeparin
- [ ] Reviparin
- [ ] Other, please specify…. _____

28. What was the dose and timing of LWMH?

29. What DOACs have been used?

- [ ] Rivaroxaban
- [ ] Apixaban
- [ ] Edoxaban
- [ ] Dabigatran
- [ ] Betrixaban

30. What was the dose and timing of DOAC?

31. Have you provided compression stockings to the patient after surgery?

- ◯ Yes, until hospital discharge
- ◯ Yes, continuously for X weeks postoperatively (please, indicate) _____
- ◯ Other, namely: _____
- ◯ No

32. VTE complications

- [ ] Thrombosis/embolism
- [ ] Bleeding

☐ Other, please specify….

☐ None

☐ Unknown

33. Bleeding consequences

☐ Hospital admission

☐ Need for intervention

☐ Need for transfusion

☐ Death

☐ Other, please specify

34. Please, indicate bleeding location

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35. Please, indicate VTE location

☐ Pulmonary embolism (PE)

☐ Deep vein thrombosis (DVT)

☐ Other, please specify...

36. VTE consequences

☐ Hospital admission

☐ Need for intervention

☐ Death

☐ Other, please specify

37. Cortisol status at the moment of VTE complication

◯ Uncontrolled CS (cortisol levels more or less unaltered)

◯ Partially controlled (significant and clinically relevant reduction)

◯ Controlled CS

◯ Other, namely: _____

38. How many days after surgery did the VTE complication occurred?
(please indicate also if VTE complication has occurred BEFORE surgery)

Please, indicate