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Abstract

Title of Study	Prospective validation of Patient Related outcome measures(PROMS) in patients with severe acute pancreatitis - SAP PROM study
Abstract and methodological description	Introduction Acute pancreatitis (AP) is a common presentation and most hospitals in the United Kingdom (UK) serving a population of 300,000 - 400,000 admit around 100 patients on a yearly basis. Severe Acute Pancreatitis (SAP), which occurs in 10% of patients is characterised by persistent organ failure and often requires critical care support and endoscopic or radiological intervention in about 40% of patients (1). Patients are sometimes in hospital for weeks to months resulting a physical, psychological & emotional upheaval; for the patient and their families (2-7). In addition, the long hospital stay and catabolic state may put these patients at risk of sarcopenia. Data from a recent Spanish prospective nationwide multicentre study showed that the proportion of patients having those outcomes are single organ failure, multiorgan failure & infected necrosis are 4%, 7% & 4% respectively(8), so clinical trials aiming to detect a reduction in such rare events would need the recruitment of thousands of patients, which may not be feasible. For this reason, new validated outcomes are needed.

On the other hand, the opinion of patients, who are at the centre of NHS healthcare, must be considered. There is a low level of agreement between the impact of disease on functional status from the patients' and physician's perspective. The NHS which aims to achieve a person-centred coordinated care; should systematically measure patient outcome associated with it (patient-reported outcome measures, PROMs). PROMs are validated instruments that patients complete reporting their status of health condition, without interpretation of the patient's response by a clinician & are increasing used in the recent years for their ability to bridge the gap between the perceptions of the clinician and patients (9, 10). The information obtained is used to adjust treatment and care and to achieve better results, enhance adherence, increase patient satisfaction, quality of life and rethink how healthcare is organised and delivered.

The recently published PAN PROMISE study studied 524 patients with AP & developed and validated the first PROMs in AP in an international prospective cohort study (2). However there is paucity of data on PROMs in patient with SAP & it is unknown how PROM's change during the course of their treatment and hospital stay. In addition, the PAN PROMISE included only 8.8% patients with SAP patients with a short follow up of 15 days post discharge. There is very limited data of PROMs in patients with SAP as this group of patients may have worse long term outcomes following disease recovery (10). In addition, there is no data on PROMs in SAP from the U.K health care setting.

Sarcopenia is frequent in patients in chronic pancreatitis, however there is paucity of data on sarcopenia in SAP particularly the impact sarcopenia may have on PROMs in SAP (11).

Therefore, the aim of this study is to validate the existing PROMS specifically in a larger cohort of patients with SAP. Furthermore, the study also aims to identify the prevalence of sarcopenia in this group of patients during the course of their treatment and the impact sarcopenia may have on PROMs.

Methods

Objectives and hypotheses

This primary aim of this prospective study to longitudinally assess PROMS using the COSMIN (Consensus based standards for the selection of health measurement instruments) questionnaire and (EORTC) QLQ-C30 for patients

admitted with SAP.
The secondary aims of the study are:
1. To evaluate associations between the clinical outcomes and the two PROMs in the short-term (within 30 days) and long-term (after 3, 6 & 12 months)
2. Identify the prevalence of sarcopenia at the time presentation and during the course of their hospital stay and the impact it may have on PROMs.

Study population and location
The study population for the study will consist of patients admitted with SAP. The remote care pancreatitis service at the Freeman Hospital is a weekly MDT with 2-3 new referrals/week with SAP. The study will be performed across an additional 4 units across the UK.
Participating centres
1. Royal Surrey Hospital, Guildford
2. James cook University Hospital, Middlesborough
3. South tyneside & Sunderland hospitals Foundation Trust
4. St. James's Hospital, Leeds
PPI involvement with the regional patient interest group - Pancreas North & their opinion was as follows:
1. How important and crucial is patient related outcome measures in patients with severe acute pancreatitis (SAP) ?
Patients that suffer from SAP all have a different story to tell about treatment path and recovery, it can be a very long, painful journey. It is therefore vital to understand PROMs along that journey to enable their care to be tailored to their needs. Patients can be hospitalised for months, so not only is their physical wellbeing suffering, being in long term severe pain, there can also be a huge impact on their mental wellbeing. Patients can suffer PTSD, family worries if they have dependants, as well as financial worries if they are not able to continue to work. We believe that tailoring patient care will bring enormous benefits to patient’s recovery.
2. What is the impact in the quality of daily life in patients with SAP?
The quality of life in patients with SAP is severely diminished, they suffer high levels of constant pain, feel nauseous, struggle to eat therefore feel very weak, and they can no longer function in their usual life. This can continue for years so patient’s lifestyle can be severely affected, losing employment is

commonplace, losing friendships and support as they can no longer socialise in their usual way and this can all have a big impact on mental wellbeing and relationships.
3. How will this study address the unmet need for patients with SAP ?
The first step of meeting a patients needs is understanding what they are in the first place. This study will be the first step in improving patient care by understanding their needs along their treatment pathway. Pancreas North are delighted that research is focussing on areas that are important to the patient and strongly support this study as it goes one step further and is focussing on what is important to the individual, this can only have a positive impact on patient care.

Inclusion criteria
All patients with SAP based on Revised Atlanta Criteria.
Eligibility criteria
Inclusion criteria
1 Age> 18 years
2. Informed consent provided
3. Severe acute pancreatitis as per the revised Atlanta classification
Eligibility criteria
Lack of informed consent

Sample size calculation
No sample size guidelines exist for assessment of PROMS and HRQOL in pancreatitis. SAP includes ~ 10% of all cases of pancreatitis. The regional annual incidence of pancreatitis is 1500 cases of which 130 cases with SAP are referred to our unit with SAP. There will also be an attrition rate of 20% as many of the patients will be in intensive care and unable to consent. Therefore, the aim is to include 50 consecutive patients with SAP from various UK centres, so a heterogeneous and regionally diverse group of patients are included in the study.

Statistical analysis
Data will be analysed using SPSS for Windows version21.0 (SPSS Inc., Chicago, IL, USA). Continuous variables will be expressed as median (IQR – interquartile range) unless specified otherwise. Categorical variables will be expressed as absolute number. The patient characteristics and outcomes will be described for the whole cohort and for the different subgroups divided according to tumour entity with appropriate descriptive statistics (mean, standard deviation, median, IQR, minimum and scores, or absolute and relative frequencies in case of categorical data. To analyse the complications and the set of PROMS and HRQoL subscales & sarcopenia dataset in the short- and long-term, Spearman's rank-correlation coefficients will be calculated and analysis of variance will be performed.

Sarcopenia assessment
Sarcopenia assessment will be undertaken during admission based on the admission CT scan. The sarcopenia assessment during follow up will be undertaken based on the follow up CT scans. It is likely the timing of the CT scans will not exactly correlate with the timing of the PROMS and HRQOL questionnaire; however, any CT imaging undertaken close to the PROMS and HRQOL time points (discharge, 3 months, 6 months and 12 months) will be included for sarcopenia assessment(including grip strength) in a longitudinal fashion(12,13).

Study duration, schedule and data collection
Patient's with confirmed SAP as per the revised Atlanta classification will be recruited into the study. Consenting for the study will be obtained on admission. All consented patients will be asked to complete the PROMs (appendix 1) and HRQOL questionnaire (appendix 2). The data collection will be led by a research nurse.
The duration of the study for each patient is 12 months including follow-up. The total duration of the overall study is expected to be 24 months.

There is limited data on PROMs and its validity in acute situations. The results from this study may provide a valuable insight on PROMs during their treatment and identify PROMs important to patients and health care providers

at various time points during their treatment which will enable improved and personalised care. Furthermore, the impact of sarcopenia on PROMS will be prospectively assessed for the first time in the literature.

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Appendix 1

Each item is scored from 0 to 10 (worst score in the last 24h, 0: none, 10: the highest
possible intensity)
1. Severe pain (abdomen, chest)
2. Abdominal bloating (stomach bloat, intestinal gas, impaired stomach emptying)
3. Back pain
4. Constipation
5. Vomiting
6. Nausea
7. Bad taste in the mouth
8. Sweating
9. Fluid retention
10. Fever
11. Yellowing of skin/jaundice
12. Dry mouth, thirst
13. Hunger
14. Weakness, lack of energy, severe tiredness
15. Muscular fatigue
16. Difficulty eating, digestive problems with foods
17. Concern for eating, concern about what to eat and what not to eat
18. Concern about possible pain recurrence
19. Hyperglycaemia (increased blood sugar, diabetes)
20. Nightmares

Appendix 2 – EORTC QLQ-C30 -

	EORTC QLQ-C30 (version 3)https://www.eortc.org › uploads › sites › 2018/08

Timetable

Name	Visit 1. During inpatient stay within 1 week After informed consent, the following data items will be collected during visit 1: a.) demographic data; b.) baseline clinical data c.) medical histor
Date	At diagnosis

Name	Visit 2: On discharge a.) complications b) interventions b.) PROMS c.) HRQOL according to EORTC QLQ-C30 c) Sarcopenia assessment
Date	At discharge

Name	Visit 3: 3 months – telephone interview a.) PROMS b.) HRQOL according to EORTC QLQ-C30 d) Sarcopenia assessment
Date	3 months after discharge

Name	Visit 4: 6 months – telephone interview a.) PROMS b.) HRQOL according to EORTC QLQ-C30 c) Sarcopenia assessment
Date	6 months after discharge

Name	Visit 5: 12 months - telephone interview a.) PROMS b.) HRQOL according to EORTC QLQ-C30 c) Sarcopenia assessment
Date	12 months after discharge

Funding

Name	total research costs = 9916
Amount	11735.0

Details of ethical approval

The study protocol is approved by Newcastle Joint Research Office (Ref no: nuth823). The study will be conducted in the context of Good Clinical Practice and in accordance with the Declaration of Helsinki. The patients will be explained the rationale behind the study. Ethics approval is in process.

Institutional approval information

The study will be sponsored by NUTH NHS Foundation trust

Declaration

Confirm Declaration: Yes

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< Back to applications (/admin/pump-priming/2/applications/)