PCRC Proposal Cover Sheet – PLATA 2

Title:

Phantom **L**imb pain **A**fter major amputation: **T**he Patterns of **A**nesthesia **(PLATA 2)**

Principal Investigator:

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Co-Investigators:

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Approved by Mentor:

Philipp Lirk MD PhD

Type of Study:

Retrospective patterns of practice study.

Hypothesis:

Perioperative use of Regional Analgesia (Epidural, Peripheral nerve block) increases over time in patients undergoing Major Limb Amputation.

Number of Patients:

Approximately 8000.

Power Analysis:

The preliminary search in the MPOG database revealed that approximately 8.000 cases will be available for analysis.

Proposed statistical test/analysis:

This is a retrospective, multi-centre trial comparing the patterns of anesthesia practice for patients undergoing major amputations under intraoperative

- Regional analgesia (epidural, peripheral nerve block)
- Multimodal analgesia (non-opiate analgesia beyond paracetamol and COX-2 inhibitors; e.g., ketamine) or
- Systemic opiate-based analgesia

from January 2010 until March 2016. Analysis will be performed on a per protocol basis.

Resources (Brief summary of resources for data collection, personnel, financial):

The online database will be programmed and maintained by the research informatician Dave Vittali, using a Web Access Database. Statistical analysis will be performed by Lotte Terwindt MD with the help of Susanne van Dieren PhD. No patient contact or additional chart review on the part of participating centers is necessary.

Our research team comprises one PI (Philipp Lirk), one Research Associate (Lotte Terwindt), one informatician (Dave Vittali), one statistician / epidemiologist (Susanne van Dieren), and two Senior Researchers (Fabian Kooij, Markus Hollmann).

Introduction

What is the significance of the clinical problem being addressed?

The collective of patients featuring critical limb ischemia is large and growing. For the population aged 60-90 years, the prevalence is estimated at 1% and growing.[1] Current literature suggests that about 25% of these patients will need to undergo amputation.[2] Even with the increased use of interventional treatments for vascular disease, amputation remains a frequently performed surgery with a frequency of approx. 190 / 100.000 / year,[3] [4] and for the United States alone, current projections estimate that the number of patients living with loss of a limb due to vascular disease will rise from the current 850.000 to 2.200.000 by the year 2050.[5]

The prevalence of phantom pain following surgical amputation is high. A recent study confined to patients undergoing lower limb amputation for peripheral vascular disease reported phantom limb pain in 79% of patients.[6] Other survey data describes figures around 75%.[7] For amputations incurred during wartime, reports from the U.S. Department of Veteran Affairs cite similar numbers (72-76%).[8] On

the other hand, traumatic amputation or amputation at early age is associated with a decreased incidence of phantom limb pain.[9]

Despite the growing importance of phantom limb pain following amputation, there is no consensus or robust evidence-base how to best minimize risk of chronic post-amputation pain.[10] Several recent publications have implicated preamputation pain and acute postsurgical pain in the development of chronic phantom limb pain, but no direct prospective randomized investigations sufficiently powered have been carried out.[11] Currently, our centre is coordinating a multicentre prospective randomized controlled trial to evaluate the efficacy of peripheral nerve block to prevent phantom limb pain after transtibial amputation (The PLATA Study).[12] However, this study is projected to last for at least another 1.5 years, including one-year follow-up. In the meantime, we plan on undertaking this retrospective study to investigate patterns of practice over time.

What current gaps exist in the understanding of this problem?

Current literature is plagued by small numbers of enrolled patients,[13] and frequent mixing of patient populations. The efficacy of perioperative interventions to prevent phantom limb pain remains equivocal. The trials reporting the least incidence of chronic phantom limb pain had instituted strict perioperative pain control, but the numbers of enrolled patients are by far too small to draw evidence-based conclusions. The hypothesis that may cautiously be formed is that optimized perioperative analgesia possibly confers significant protection against phantom limb pain, perhaps with an added advantage when combined with regional anesthesia. However, neither patterns of practice, nor efficacy of different perioperative interventions are known at this timepoint.

How will this project address this gap and advance clinical care and/or research knowledge?

This project will close the knowledge gap by analyzing a large number of patients retrospectively, determining

- Anesthetic practice patterns for amputation surgery and
- Characteristics of patients undergoing different types of amputation.

Methods

The present research project seeks to employ retrospective patterns of practice analysis. Specifically, we will analyze practice patterns and patient characteristics for the patients in the MPOG database.

Study type

Retrospective patterns-of-practice study.

Primary outcome

- Practice patterns for amputation surgery (general anesthesia, spinal anesthesia, epidural anesthesia, peripheral nerve block, combinations).

Secondary outcome(s), where applicable

- Demographics of patients undergoing surgery (age, gender, ASA status, comorbidities [cardiac, diabetic, hypertensive, renal, …], site of surgery).

Patient inclusion criteria

All patients in the MPOG database having undergone amputation surgery in one of the participating centers from January 2010 until July 2015.

Patient exclusion criteria

Evaluation of Practice patterns and Demographics: None.

Data source

- Practice patterns and Demographics: MPOG database (existing data).

Statistical analysis

This is a retrospective, patterns of practice investigation comparing the incidence of regional anesthesia in patients undergoing major amputations.

- All parameters will be summarised using descriptive statistics, i.e. number (%) of patients for categorical variables and mean, SD (standard deviation), median, minimum/maximum for continuous variables. Descriptive statistics will be produced by treatment group. No formal hypothesis testing will be performed. Appropriate statistical tests will be applied in an explorative manner only.
- Analysis of variance or Kruskal-Wallis test will be used to analyse variables such as postoperative highest and average pain scores.

Power analysis

- The preliminary search in the MPOG database revealed that approximately 8.000 cases will be available for analysis.

Variables to be collected

Source	Data Column	Data type	Source table, column, and concept
MPOG preoperative data	Age in years	Numeric, 0-150	Aims_intraopcaseinfo.AIMS_age_in_years
	Gender	Character	Aims_patients.AIMS_sex
	Home medications	Character	Aims_preop, MPOG concept ID 70079
	ASA score, Body Mass Index	Numeric, 0-5, 0-100	Aims_preop, MPOG concept ID 70233, 70253
	Comorbidity - COPD	Binary (yes/no)	Preoperative observations, MPOG concept 70115
	Comorbidity – Hypertension or Diabetes Mellitus	Binary (yes/no)	Preoperative observations, MPOG concepts 70031, 70046
	Comorbidity – Renal failure	Binary (yes/no)	Preoperative observations, MPOG concept 5002
	Comorbity – Hepatic failure	Binary (yes/no)	Preoperative observations, MPOG concept 70052
	Comorbidity – Previous myocardial infarction	Binary (yes/no)	Preoperative observations, MPOG concept 70033
	Comorbidity – Previous stroke	Binary (yes/no)	Preoperative observations, MPOG concepts 70086, 70088
MPOG surgical data			ICD codes, billing data

MPOG practice pattern data	Type of anesthesia: nerve block	Binary (yes/no)	Intraoperative Events, Interventions and Observations, MPOG concept 3015
	Type of anesthesia: type of block		Intraoperative Events, Interventions and Observations, MPOG concepts for different nerve blocks
	Type of anesthesia: catheter placed	Binary (yes/no)	Intraoperative Events, Interventions and Observations, MPOG concept 50021
	Type of anesthesia: spinal	Binary (yes/no)	Intraoperative Events, Interventions and Observations, MPOG concept 50680
	Type of anesthesia: epidural	Binary (yes/no)	Intraoperative Events, Interventions and Observations, MPOG concept 50643
	Type of anesthesia: CSE	Binary (yes/no)	Aims_intraopphysiologic, MPOG concept 50614
	Type of anesthesia: General	Binary (yes/no)	Defined by presence of airway management device: LMA (50209), Tube (50671)
MPOG intraoperative data	Type of analgesia	Binary (yes/no)	Intraoperative medications, MPOG concept 10238 and 11060
MPOG postoperative data	Highest and average postoperative pain scores	Numeric, 0-10	Intraoperative events, MPOG concept 50776

Queries

```
/*
These are the queries used for the PLATA2 study. The queries retrieve the requested data for each
MPOG table seperately. Selection of cases is done by selecting on all "amputation ICD codes" and
the inclusion criteria concerning the dates of surgery.
*/
-----------------------------------------------------------------------------------------------------------------
-- select information from mpog_mas..aims_intraopcaseinfo
--                    - Patient age in years
-----------------------------------------------------------------------------------------------------------------

select mpog_case_id, aims_patient_age_years from mpog_mas..aims_intraopcaseinfo
where mpog_case_id in
-- Select the cases with amputation procedure codes
(select mpog_case_id from mpog_mas..aims_billingprocedures where
Aims_Procedure_Code like '%0X6%' or AIMS_Procedure_Code like '%0Y6%')
and
-- Select the cases in which anesthesia started on or after January 1st. 2010 and before August 1st. 2015
mpog_case_id in
(select mpog_case_id from mpog_mas..aims_intraopnotes where mpog_note_concept_id = 50002
and aims_note_observation_dt >= '20100101' and aims_note_observation_dt < '20150801')

-----------------------------------------------------------------------------------------------------------------
-- select information from mpog_mas..aims_patients
--                    - Patient gender
-----------------------------------------------------------------------------------------------------------------
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```
select caseinfo.mpog_case_id, patients.aims_sex from mpog_mas..aims_intraopcaseinfo caseinfo
left join mpog_mas..aims_patients patients
on patients.MPOG_Patient_ID = caseinfo.MPOG_Patient_ID
where mpog_case_id in
-- Select the cases with amputation procedure codes
(select mpog_case_id from mpog_mas..aims_billingprocedures where
Aims_Procedure_Code like '%0X6%' or AIMS_Procedure_Code like '%0Y6%')
and
-- Select the cases in which anesthesia started on or after January 1st. 2010 and before August 1st. 2015
mpog_case_id in
(select mpog_case_id from mpog_mas..aims_intraopnotes where mpog_note_concept_id = 50002
and aims_note_observation_dt >= '20100101' and aims_note_observation_dt < '20150801')

-------------------------------------------------------------------------------------------------------------------------

-- select information from mpog_mas..aims_preop
--                    - Preoperative information

-------------------------------------------------------------------------------------------------------------------------

select * from mpog_mas..aims_preop where mpog_preop_concept_id in (70079, 70253, 70233, 70115,
70031, 70060, 70052, 70033, 70046, 70086, 70088)
and
mpog_case_id in
-- Select the cases with amputation procedure codes
(select mpog_case_id from mpog_mas..aims_billingprocedures where
Aims_Procedure_Code like '%0X6%' or AIMS_Procedure_Code like '%0Y6%')
```

```
and
-- Select the cases in which anesthesia started on or after January 1st. 2010 and before August 1st. 2015
mpog_case_id in
(select mpog_case_id from mpog_mas..aims_intraopnotes where mpog_note_concept_id = 50002
and aims_note_observation_dt >= '20100101' and aims_note_observation_dt < '20150801')

-----------------------------------------------------------------------------------------------------------------------
-- select information from mpog_mas..aims_intraopnotes
--                  - Types of anesthesia used
--                  - Postoperative pain scores
-----------------------------------------------------------------------------------------------------------------------

select * from mpog_mas..aims_intraopnotes where mpog_note_concept_id in
(50356,50383,50384,50385,50386,50387,50388,50389,
50398,50635,50690, 50021, 50680, 50643, 50614, 50209, 50671, 50776)
and
mpog_case_id in
-- Select the cases with amputation procedure codes
(select mpog_case_id from mpog_mas..aims_billingprocedures where
Aims_Procedure_Code like '%0X6%' or AIMS_Procedure_Code like '%0Y6%')
and
-- Select the cases in which anesthesia started on or after January 1st. 2010 and before August 1st. 2015
mpog_case_id in
(select mpog_case_id from mpog_mas..aims_intraopnotes where mpog_note_concept_id = 50002
and aims_note_observation_dt >= '20100101' and aims_note_observation_dt < '20150801')
```

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-- select information from mpog_mas..aims_sites

--                  - epidurals (50643 and 100312 and 100021)

--                  - tracheal tube (50671)

-----------------------------------------------------------------------------------------------------------------------


select * from mpog_mas..aims_sites where mpog_site_type_id in (50671, 50643, 100312, 100021)

and

mpog_case_id in

-- Select the cases with amputation procedure codes

(select mpog_case_id from mpog_mas..aims_billingprocedures where

Aims_Procedure_Code like '%0X6%' or AIMS_Procedure_Code like '%0Y6%')

and

-- Select the cases in which anesthesia started on or after January 1st. 2010 and before August 1st. 2015

mpog_case_id in

(select mpog_case_id from mpog_mas..aims_intraopnotes where mpog_note_concept_id = 50002

and aims_note_observation_dt >= '20100101' and aims_note_observation_dt < '20150801')


-----------------------------------------------------------------------------------------------------------------------

-- select information from mpog_mas..aims_intraopmedications

--                  - Ketamine and S-Ketamine

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select * from mpog_mas..aims_intraopmedications where mpog_med_concept_id in (10238, 11060)

and
```

```
mpog_case_id in
-- Select the cases with amputation procedure codes
(select mpog_case_id from mpog_mas..aims_billingprocedures where
Aims_Procedure_Code like '%0X6%' or AIMS_Procedure_Code like '%0Y6%')
and
-- Select the cases in which anesthesia started on or after January 1st. 2010 and before August 1st. 2015
mpog_case_id in
(select mpog_case_id from mpog_mas..aims_intraopnotes where mpog_note_concept_id = 50002
and aims_note_observation_dt >= '20100101' and aims_note_observation_dt < '20150801')

-----------------------------------------------------------------------------------------------------------------------
-- select billig information
-----------------------------------------------------------------------------------------------------------------------

select * from mpog_mas..aims_billingdiagnoses
where mpog_case_id in
-- Select the cases with amputation procedure codes
(select mpog_case_id from mpog_mas..aims_billingprocedures where
Aims_Procedure_Code like '%0X6%' or AIMS_Procedure_Code like '%0Y6%')
and
-- Select the cases in which anesthesia started on or after January 1st. 2010 and before August 1st. 2015
mpog_case_id in
(select mpog_case_id from mpog_mas..aims_intraopnotes where mpog_note_concept_id = 50002
and aims_note_observation_dt >= '20100101' and aims_note_observation_dt < '20150801')
```

```
select * from mpog_mas..aims_billingprocedures

where mpog_case_id in

-- Select the cases with amputation procedure codes

(select mpog_case_id from mpog_mas..aims_billingprocedures where

Aims_Procedure_Code like '%0X6%' or AIMS_Procedure_Code like '%0Y6%')

and

-- Select the cases in which anesthesia started on or after January 1st. 2010 and before August 1st. 2015

mpog_case_id in

(select mpog_case_id from mpog_mas..aims_intraopnotes where mpog_note_concept_id = 50002

and aims_note_observation_dt >= '20100101' and aims_note_observation_dt < '20150801')
```

Management of missing data

Missing data will be described in the final analysis, no attempts will be made to impute or retrieve missing data.

References

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