**TXP\_南東北　脈圧の研究・計画書**

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**Title**: Association of pulse pressure with cardiovascular diseases in the emergency department

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**Background:**

救急外来においてacute cardiovascular eventsは鑑別すべき重要な疾患である。acute cardiovascular eventsとsepsisはカテコラミンの放出を起こし、vital signs、特に脈圧に影響を与えることが知られている。しかし過去の報告では脈圧がin-hospital mortalityに関連するのはわかっているが(?)、心血管系疾患を鑑別する能力があるかどうかはわかっていない。

**What’s known**

Pulse pressure (PP), defined as the difference between systolic and diastolic blood pressure (SBP and DBP), is affected by both arterial stiffness and ventricular ejection.

According to a major textbook on physical examination, the difference between systolic and diastolic pressure is often greater than 50% of the systolic pressure, without being considered abnormally wide (Orient, Jane. Sapira's Art & Science of Bedside Diagnosis (pp. 118-119). Wolters Kluwer Health. Kindle Edition). Several studies reported the importance of PP on the \*\* \*\*\*.

An extremely widened pulse pressure [i.e., (SBP − DBP) > 50% SBP] may be seen in conditions associated with myocardial infarction, dissecting aneurysm, or massive pulmonary embolism. a high stroke volume, such as aortic regurgitation, hyperthyroidism, fever, or anemia (Orient, Jane. Sapira's Art & Science of Bedside Diagnosis (pp. 118-119). Wolters Kluwer Health. Kindle Edition).

上記はおそらくエキスパートオピニオンで、詳しく調べた研究はない。

**Knowledge gap**

・prediction ability of PP at emergent department (ED) triage to differentiate patients with cardiovascular diseases such as myocardial infarction, dissecting aneurysm, or massive pulmonary embolism cardiovascular disease ± critical conditions（sepsis）

＊心血管系だけに絞って、循環器系の雑誌に出すのもあるかも。心血管だけに絞ると、Referenceに敗血症が入ってしまい、効果量が少なくなる。

・A reference value of 65 mmHg (50 mmHg ± 2 SD) was assessed at check-up2, not at ED.

**Study aim:** We will aim to investigate the association of pulse pressure with the diagnosis of acute cardiovascular events among patients who visited ED for medical reasons.

Sapira（教科書）では、大脈圧＝PP>1/2\*SBPとなっているが、この定義ではバイナリ（0か1）になってしまい情報のロスがもったいない→今回はPP index = PP/(1/2 \* SBP)とし、これを説明変数として解析する。

1. PP indexを10等分し、low PP index〜high PP indexそれぞれのカテゴリに含まれる疾患をICD-10で列挙。またPP indexと入院・死亡の関係を見ることでPP indexと患者アウトカムの全体像を見る（過去の研究があればvalidationとする）。

2. chest pain/syncope/nausea/headacheなどの主訴で受診した患者とacute cardiovascular diseasesとの関連を見る（まずは全患者で見て、次に主訴で絞る）。

3. feverで受診した患者の中からsepsisとの関連を見る（これも同様に全患者でみて、次に主訴で絞る）。主訴が悪寒戦慄、診断がsepsisになった患者も含める。

**Methods:**

**Study design:** Retrospective observational study

**Study period:** April 1, 2018 through September 31, 2019

**Inclusion criteria:**

P: 救急外来を受診した成人患者

・組入基準：

・年齢：成人（18歳）

・疾患：内科

**Exclusion criteria:** 小児（≤17 years 17歳以下を除き、18歳以上を含める）、外傷および外因性の病態（溺水・溢頸・中毒）、心肺停止および蘇生後の患者

**Data collection:**

・救急外来でのバイタルサイン（呼吸数、心拍数、SpO2、血圧、体温）

・主訴、既往歴

・最終診断

**Primary outcome:**

**Acute cardiovascular diseases**

AMI: I21.x

STEMI: I21.0, I21.1, I21.3

NSTEMI: AMI, but not STEMI

UAP: I20.0

1. Acute heart failure:

Aortic dissection: I71.0, I71.1, I71.3, I71,5 , I71.8

Other acute ischaemic heart diseases I240 (I240A, I241, I248, I248A, I249)

Pulmonary Embolism: I26.x

Subarachnoid haemorrhage I600 (I601, I602, I603, I604, I605, I606, I606A, I606B, I606C, I607, I607A, I608, I609, I609A)

Intracerebral haemorrhage I610 (I611, I611A, I611B, I6612, I613, I614, I615, I616, I618, I619)

Other non-traumatic intracranial haemorrhage I620 (I621, I629)

Cerebral infarction I630 (I631, I632, I633, I634. I635, I636, I638, I639)

Stroke, not specified as haemorrhage or infarction I640 (I649)

**Statistical analysis:**

1. PP indexを10等分してそれぞれのカテゴリにおけるdiagnosisとdispositionを見てみましょうか

・inclusion, exclusionのフロー　心肺停止は除外　cardio, sepsis以外でも、急性呼吸不全もppが上がるので、効果量が少なくなるかも。Asthmaの発作とか

・Table 1 患者の情報

・図表　pp indexの10等分と、top10のdiagnosis

・pp indexの10等分　それぞれ入院と死亡の割合　lowess curve

・カテコラミンリリースを伴う疾患: 呼吸不全（\*\*, \*\*, \*\*）, 心不全, ショック（\*\*, \*\*, \*\*）

・低血糖

・敗血症

＊今回はcardiovascularに絞るか、敗血症も含めるか、まだ議論の余地あり。

**＊ cardiovascular disease: 今回は急性心不全、ACS、解離などが対象、不整脈は除く。**

**“acute emergency cardiovascular disease”でpubmedかgoogle検索し、先行研究ではどのICD10コードで拾っているか調べる。**

1) rheumatic heart disease (ICD-10 code: I01-I09), 2) hypertensive heart disease (ICD-10 code: I10-I13), 3) ischemic heart disease (ICD-10 code: I20-I25), 4) cerebrovascular disease (ICD-10 code: I60-I69), 5) inflammatory heart diseases (ICD-10 code: I30-I33, I38, I40, I42), and 6) other cardiovascular diseases (ICD-10 code: I00, I26-I28, I34-I37, I44-I51, I70-I99)

●cardiovascular diseases (ICD-10: I00-I99, G45, G46, M30, M31, R58)

<https://doi.org/10.1371/journal.pone.0183224>

●all cardiovascular causes (International Classification of Diseases, Revision 10 (ICD-10) codes I00-I99), ischemic heart disease (ICD-10 codes I20-I25), and myocardial infarction (ICD-10 code I21).

<https://www.ahajournals.org/doi/10.1161/circ.133.suppl_1.p325>

山本 まるみ先生より

●https://www.ncbi.nlm.nih.gov/pubmed/31464622

IX Diseases of the circulatory system

I00-I02, I05-I15, I20-I25, I26-I28, I30-I52, I60-I89, I95-I99

Serious cardiac conditions

Cardiac arrest: I46.x

Atrioventricular block: I44.1, I44.2

Ventricular Tachycardia: I47.0, I47.2, I47.2, I47.2

Aortic dissection: I71.0, I71.1, I71.3, I71,5 , I71.8

Pulmonary Embolism: I26.x

Pneumothorax: J93.x

●https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6839230/pdf/12913\_2019\_Article\_4674

ICD-10 codes included in study population

Acute myocardial infarction I210 (I210A, I210B, I211, I211A, I211B, I213, I214, I219) Other acute ischaemic heart diseases I240 (I240A, I241, I248, I248A, I249) Subarachnoid haemorrhage I600 (I601, I602, I603, I604, I605, I606, I606A, I606B, I606C, I607, I607A, I608, I609, I609A)

Intracerebral haemorrhage I610 (I611, I611A, I611B, I6612, I613, I614, I615, I616, I618, I619)

Other non-traumatic intracranial haemorrhage I620 (I621, I629)

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Stroke, not specified as haemorrhage or infarction I640 (I649)

急性の疾患だけを見たいので、僧帽弁閉鎖不全　これは慢性では？？acute heart failureが一番めんどくさそう。

**Secondary outcomes:**

**Statistical analysis:**

**Strengths of the current study:**

**・**救急外来の内科患者全体を対象に脈圧とアウトカムの関連を調べた先行研究はおそらくない。

・PRQと同様、主訴別の結果を出してみてもいいかもしれない

・先行研究との比較　下記の所見を引用。

PP increases slowly up to age 60 but then rises with increasing age1, because

SBP increases with age due to fibrosis of the arterial wall and atherosclerotic deposits 2,3, and DBP decreases from the age of 604.

A pulse pressure greater than a reference value of 65 mmHg (50 mmHg ± 2 SD) may be an independent predictor of cardiovascular morbidity ﻿or mortality2. High PP was reported to be a better predictor of cardiovascular disorders than SBP or DBP alone1, an independent predictor of mortality among elderly hospitalized patients5.

**Limitations:**

1. Missing data
2. 単施設　外的妥当性が低いかも

**Expected findings:**

**Target journals:**

**Timelines:**

1月　山本先生、後藤先生とCQ→RQについて話し合う

2月前半　研究計画書完成、呼吸数の研究と同じデータセットを使用して解析してみる

2月後半　最初の原稿をco-authorに提出

3月中に投稿（もし日立だけでなく、土浦など他の病院のデータも使うならもう少しかかるかも）

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