Analýza složení karotického plátu pomocí intravaskulární spektroskopie

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Kardiologická klinika 2.LF UK a FN Motol

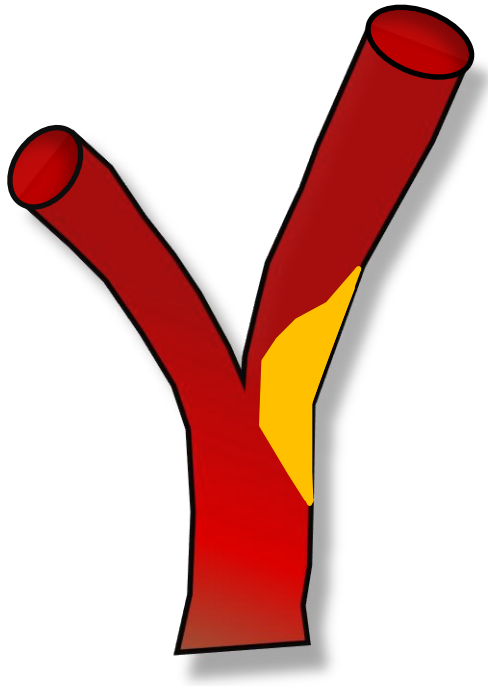
Úvod

Ateroskleróza = systémové onemocnění

Systémová expozice rizikovým faktorům

X

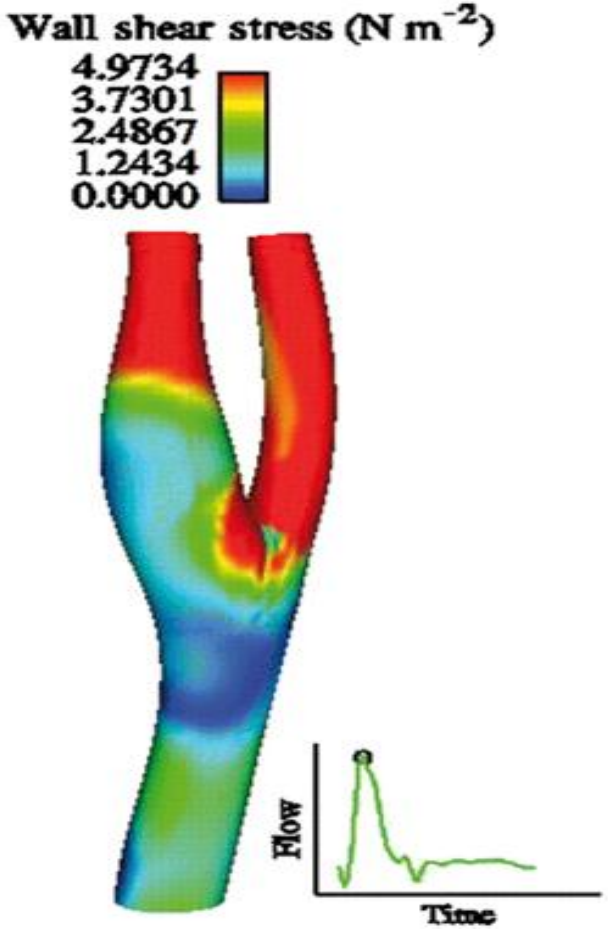
Fokální výskyt aterosklerotických plátů



Endoteliální smykové tření (ESS)

Endoteliální dysfunkce:

1. Fenotyp endotelií
2. Zvýšení permeability pro LDL
3. Snížení tvorby eNOS
4. Zvýšení oxidativního stresu
5. Aktivace prozánětlivých kaskád



Stone et al., Eur Heart Journal,2007

Hung et al., Intervent cardiol clin, 2015

Makris et al., Brit Inst Radiol 2010

Složení plátu- vysoké ESS

Int J Cardiovasc Imaging
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ORIGINAL PAPER

High wall shear stress and high-risk plaque: an emerging concept

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Abstract In recent years, there has been a significant effort to identify high-risk plaques *in vivo* prior to acute events. While number of imaging modalities have been developed to identify morphologic characteristics of high-risk plaques, prospective natural-history observational studies suggest that vulnerability is not solely dependent on plaque morphology and likely involves additional contributing mechanisms. High wall shear stress (WSS) has recently been proposed as one possible causative factor, promoting the development of high-risk plaques. High WSS has been shown to induce specific changes in endothelial cell behavior, exacerbating inflammation and stimulating progression of the atherosclerotic lipid core. In line with experimental and autopsy studies, several human studies have shown associations between high WSS and known morphological features of high-risk plaques. However, despite increasing evidence, there is still no longitudinal data linking high WSS to clinical events. As the interplay between atherosclerotic plaque, artery, and WSS is highly dynamic, large natural history studies of atherosclerosis that include WSS measurements are now warranted. This review will summarize the available clinical evidence on high WSS as a possible etiological mechanism underlying high-risk plaque development.

Keywords Acute coronary syndrome · Coronary artery disease · Computational fluid dynamics · High-risk plaque · Wall shear stress

Abbreviations

ACS	Acute coronary syndrome
CAD	Coronary artery disease
CCTA	Coronary computed tomography angiography
CFD	Computational fluid dynamics
FA	Fibroatheroma
IPH	Intraplaque hemorrhage
OCT	Optical coherence tomography
PSS	Plaque structural stress
TCFA	Thin-cap fibroatheroma
ThCFA	Thick-cap fibroatheroma
VH-IVUS	Virtual histology intravascular ultrasound
WSS	Wall shear stress

Introduction

Since the introduction of the high-risk plaque concept, th
have been significant efforts to identify high-risk plaque
vivo prior to rupture. In recent years, number of inv
and non-invasive imaging modalities have been dev
that are able to identify morphologic characteri
high-risk plaque [1]. Nevertheless, prospective na
tory observational studies using these imaging to
have consistently shown that not all plaques go t
rapid progression phase and few high-risk plaqu
rise to a clinical event [2–4]. These data sugge
vulnerability is not solely dependent on plaqu

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CLINICAL RESEARCH

EXPERIMENTAL RESEARCH

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High shear stress relates to intraplaque haemorrhage in asymptomatic carotid plaques

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Shear stress
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MRI

ABSTRACT

Background and aims: Carotid artery plaques with vulnerable plaque components are related to a higher risk of cerebrovascular accidents. It is unknown which factors drive vulnerable plaque development. Shear stress, the frictional force of blood at the vessel wall, is known to influence plaque formation. We evaluated the association between shear stress and plaque components (intraplaque haemorrhage (IPH), lipid rich necrotic core (LRNC) and/or calcifications) in relatively small carotid artery plaques in asymptomatic persons.
Methods: Participants ($n = 74$) from the population-based Rotterdam Study, all with carotid atherosclerosis assessed on ultrasound, underwent carotid MRI. Multiple MRI sequences were used to evaluate the presence of IPH, LRNC and/or calcifications in plaques in the carotid arteries. Images were automatically segmented for lumen and outer wall to obtain a 3D reconstruction of the carotid bifurcation. These reconstructions were used to calculate minimum, mean and maximum shear stresses by applying computational fluid dynamics with subject-specific inflow conditions. Associations between shear stress measures and plaque composition were studied using generalized estimating equations analysis, adjusting for age, sex and carotid wall thickness.
Results: The study group consisted of 93 atherosclerotic carotid arteries of 74 participants. In plaques with higher maximum shear stresses, IPH was more often present (OR per unit increase in maximum shear stress (log transformed) = 12.34, $p = 0.001$). Higher maximum shear stress was also significantly associated with the presence of calcifications (OR = 4.28, $p = 0.015$).
Conclusions: Higher maximum shear stress is associated with intraplaque haemorrhage and calcifications.

1. Introduction

Atherosclerosis in the carotid arteries represents an important cause of ischemic stroke [1]. The composition of atherosclerotic plaques is an important predictor for plaque rupture and subsequent thromboembolic events [2]. Plaques that contain a large lipid rich necrotic core (LRNC), intraplaque haemorrhage (IPH), inflammation and/or are covered by a thin fibrous cap are considered the most vulnerable to rupture [3–5]. Conversely, the presence of calcifications has been associated with a more stable plaque phenotype [6,7].

The development of a vulnerable plaque is a complex process which is still not completely understood. Initially, plaque size or lumen obstruction were thought of as the most important determinants of plaque vulnerability, but these explain variability in

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0021-9150/

Hypotéza

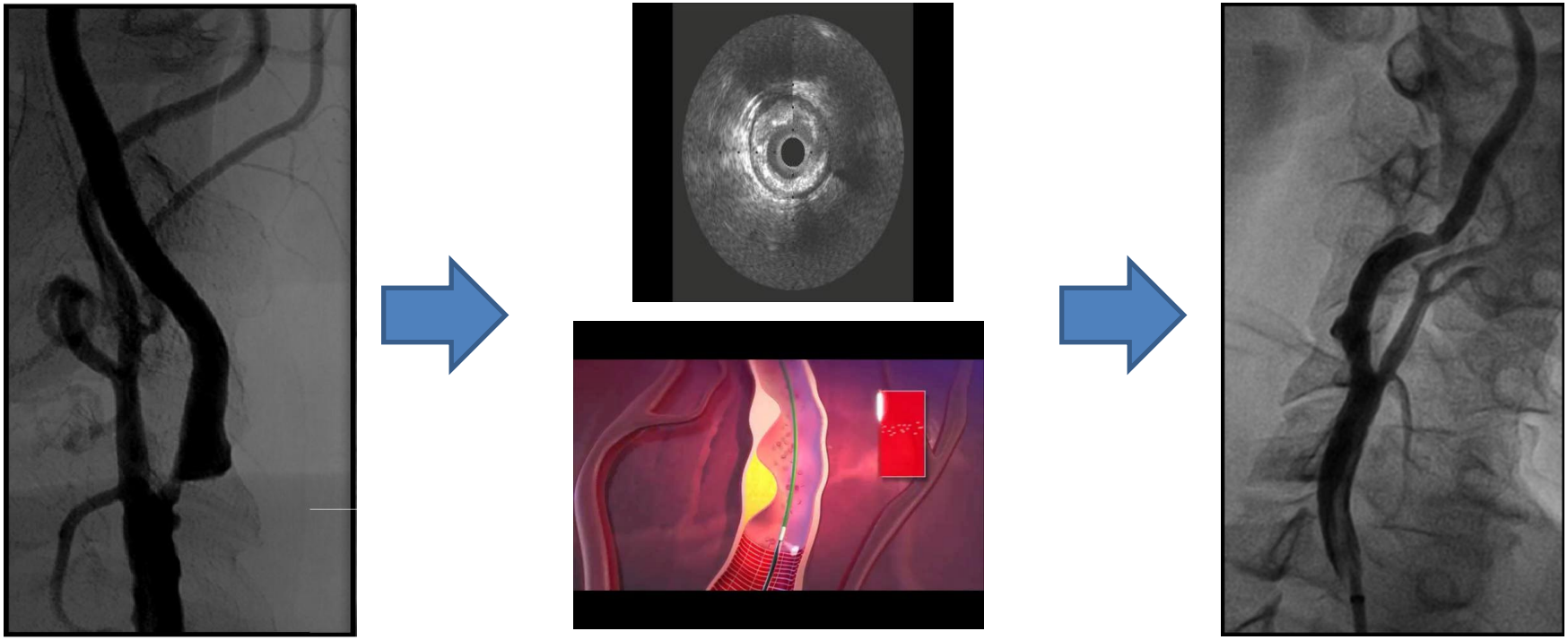
Lipidové jádro se vyskytuje častěji v **proximálním** úseku pokročilého karotického plátu.

Ku, et al. Arteriosclerosis, 1985

Cheng, et al. Circulation, 2005

Metodika

Pacientům s významnou stenózou a. carotis bylo provedeno vyšetření pomocí blízko-infračervené spektroskopie (NIRS) a intravaskulárního ultrazvuku (IVUS) před provedením karotického stentingu.

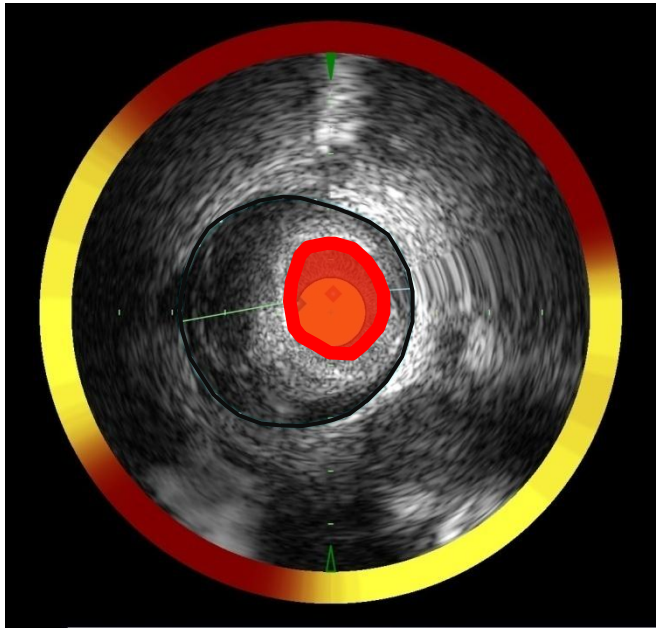


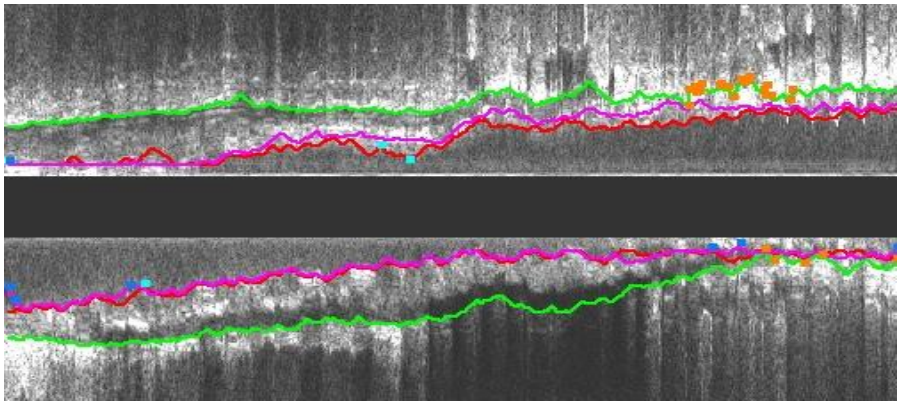
Charakteristika souboru

Počet pacientů	**105**
Počet vyšetřených tepen	**117**
Muži n/N (%)	**78/105 (68)**
Věk průměr ±SD (roky)	**67.1 ± 8.3**
BMI průměr ±SD	**28.1 ± 4.1**
Symptomatické stenózy n/N (%)	**17/105 (16)**
Arteriální hypertenze n/N (%)	**93/105 (88)**
ICHS n/N (%)	**45/105 (43)**
Nikotinismus n/N (%)	**39/105 (37)**
Diabetes mellitus n/N (%)	**36/105 (34)**
Hs-CRP (mg/l) průměr ±SD	**2.89 ± 2.29**
Kreatinin (µmol/l) průměr ±SD	**85.5 ± 26.0**
Celkový cholesterol (mmol/l) průměr ±SD	**4.36 ± 0.93**
LDL cholesterol (mmol/l) průměr ±SD	**2.47 ± 0.85**

Metodika

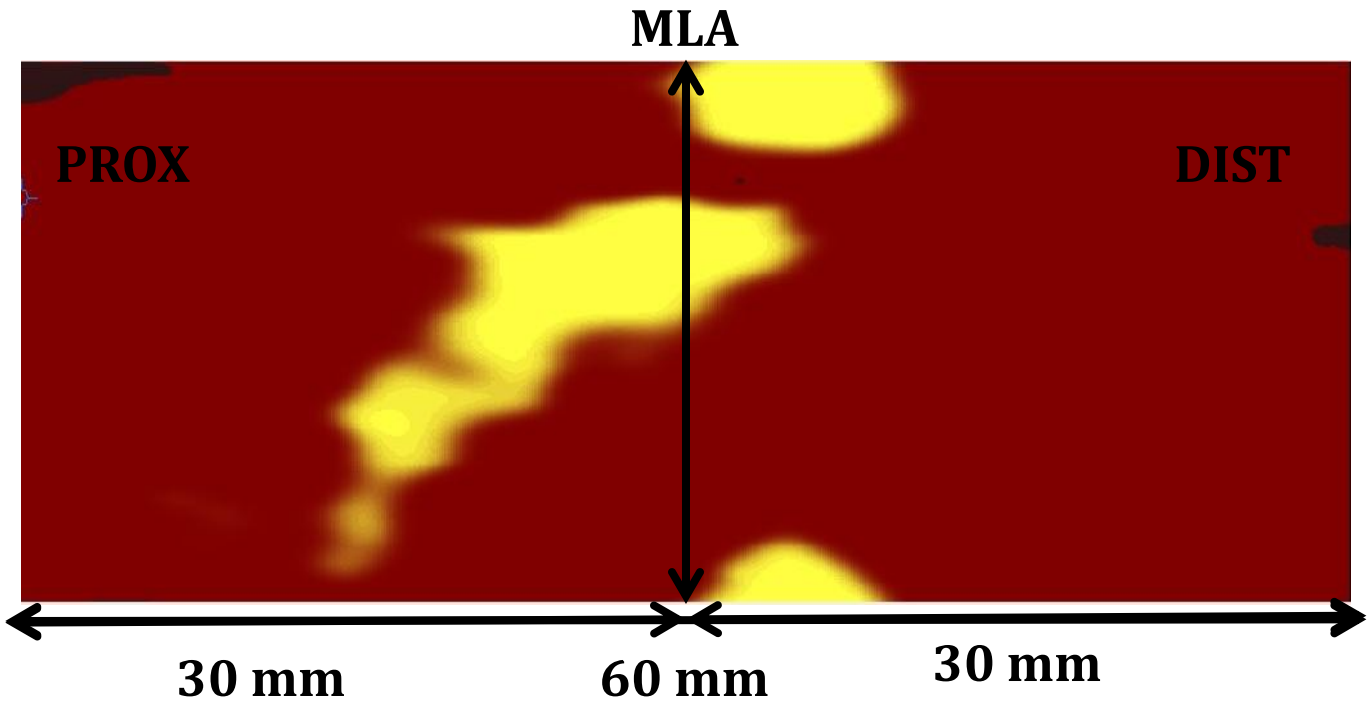
- Získaná data byla následně analyzována pomocí specializovaného softwaru (QIVUS, Medis, Leiden, NL).
- Pomocí IVUS byla nejprve určena oblast minimální plochy lumen (MLA).





Metodika

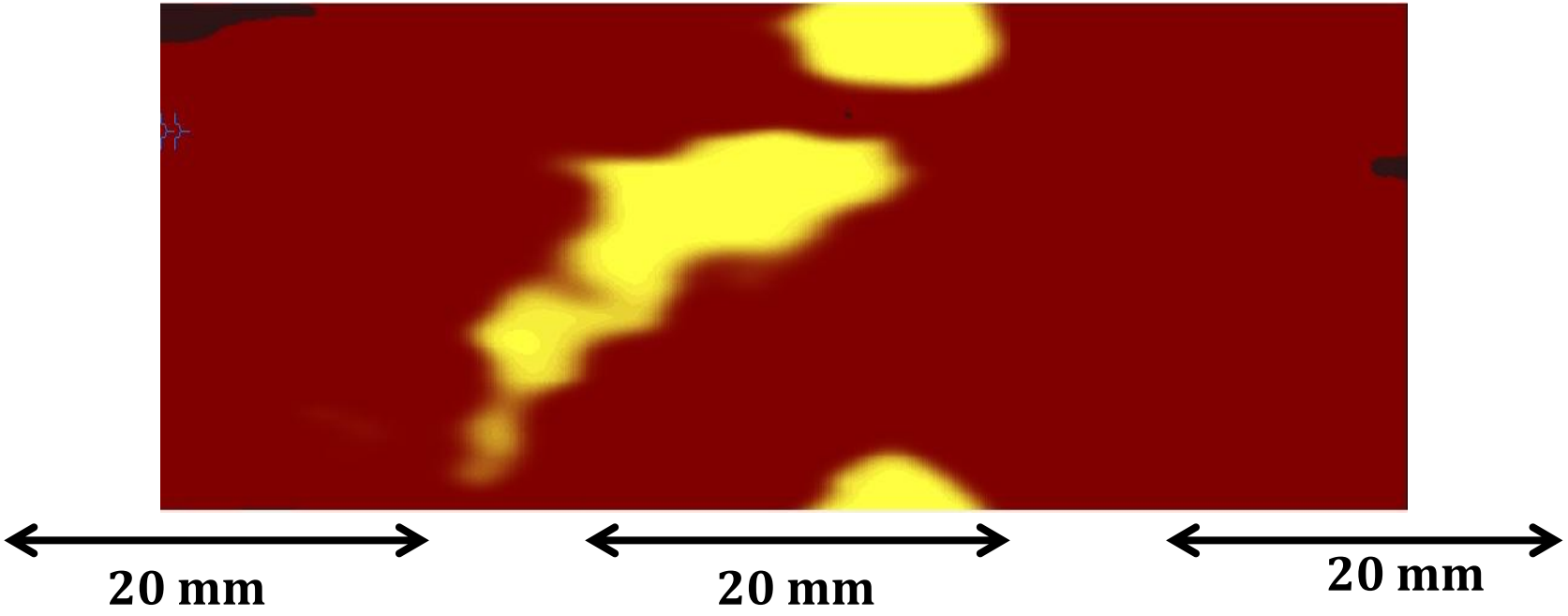
- Přítomnost lipidového jádra analyzována pomocí NIRS 30 mm směrem proximálně i distálně od MLA
- Ve 2 mm segmentech určen lipid core burden index (LCBI)



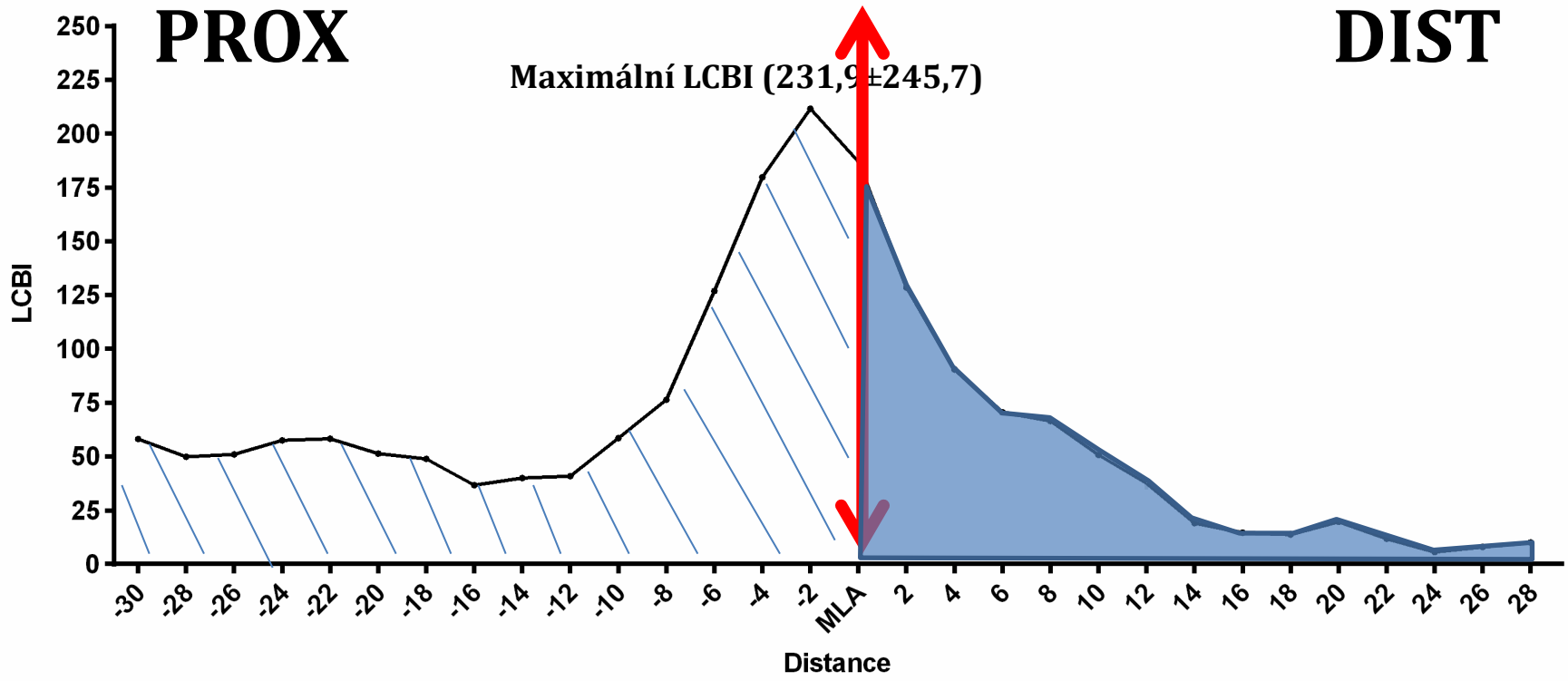
Metodika

Vyšetřená oblast byla rozdělena na tři tercily o délce 20 mm.

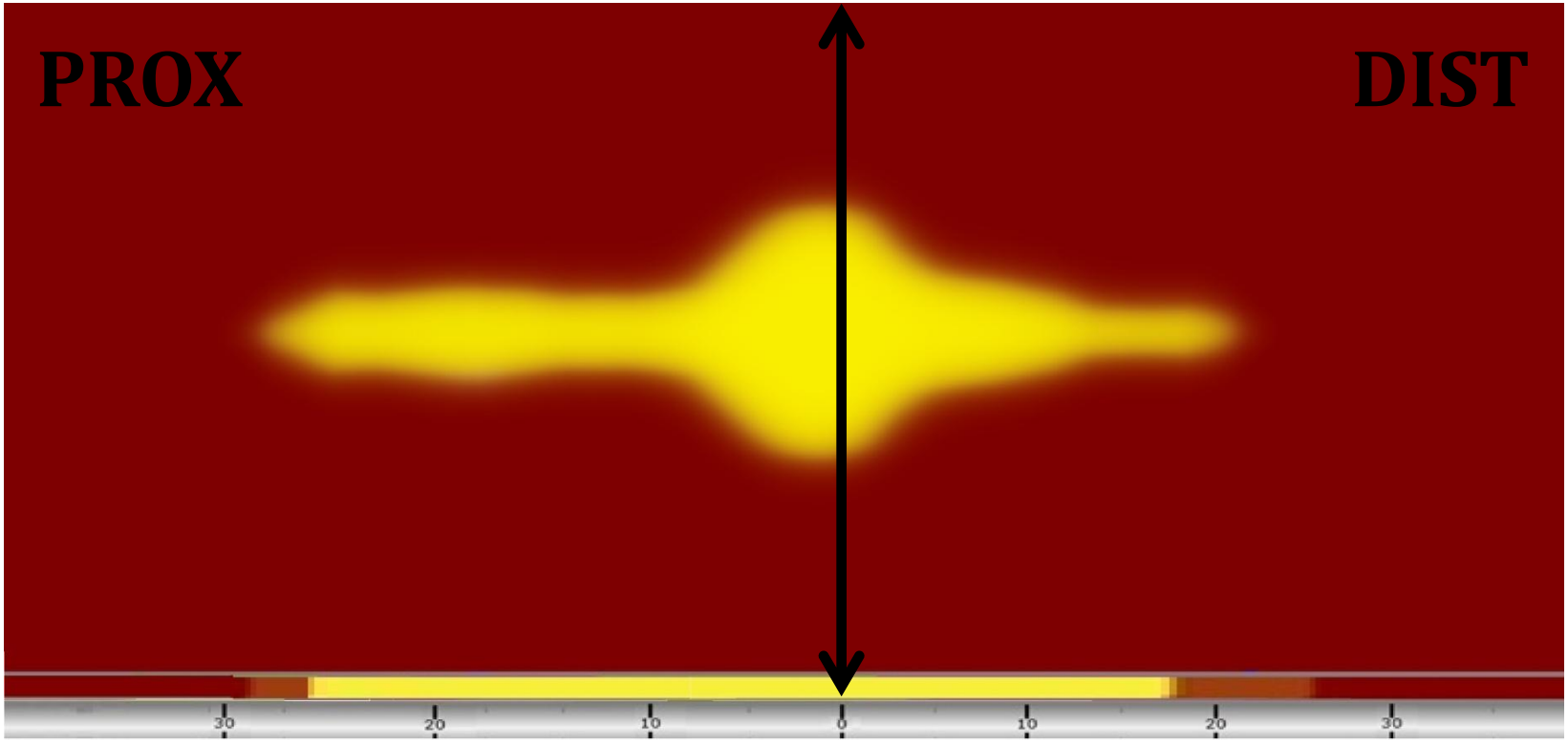
Proximální (PROX) **Střední (MID)** **Distální (DIST)**



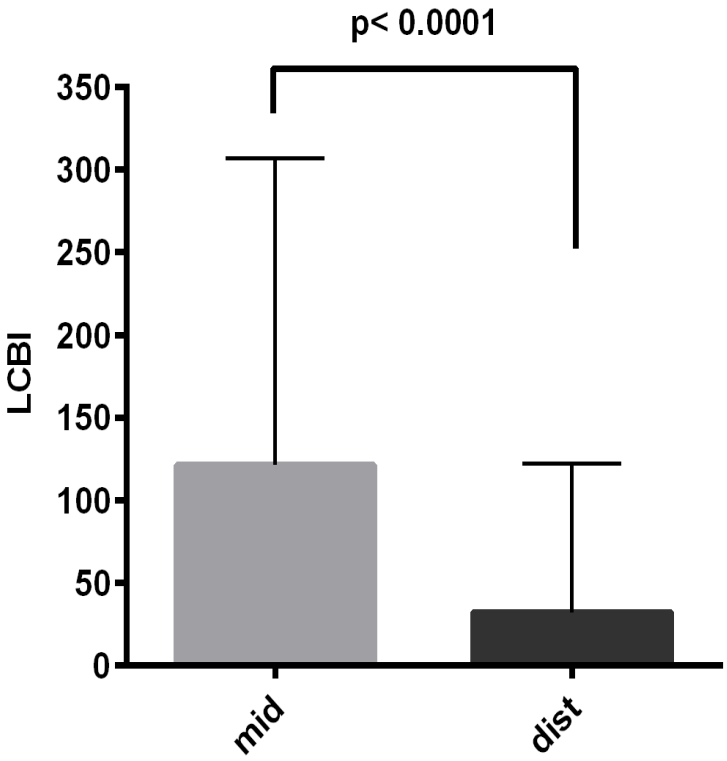
Výsledky


PROX
DIST
Maximální LCBI (231,9±245,7)
LCBI
250
225
200
175
150
125
100
75
50
25
0
-30
-28
-26
-24
-22
-20
-18
-16
-14
-12
-10
-8
-6
-4
-2
MLA
2
4
6
8
10
12
14
16
18
20
22
24
26
28
Distance

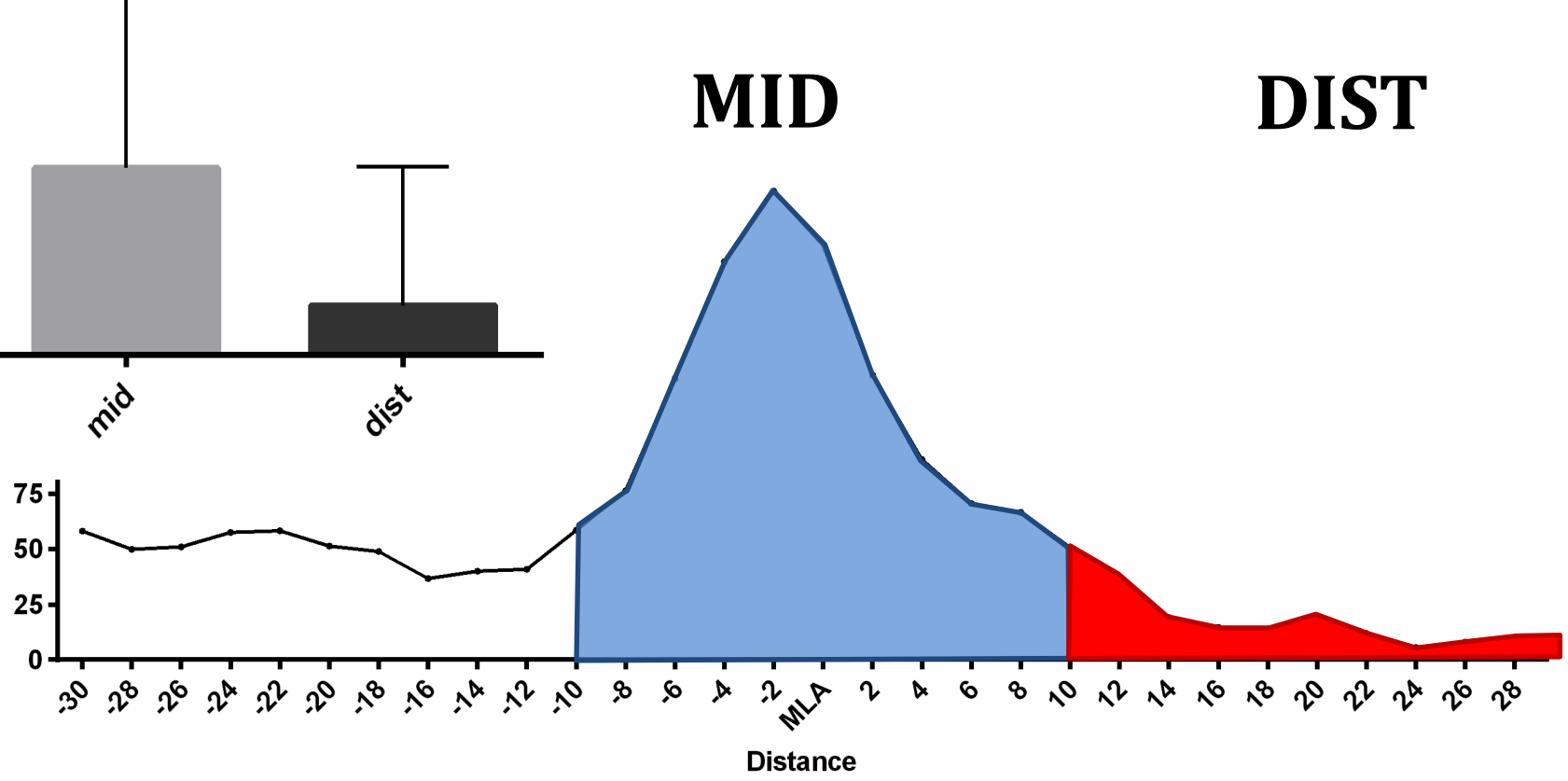
Výsledky



Průměrné LCBI bylo 96,9±165,5.

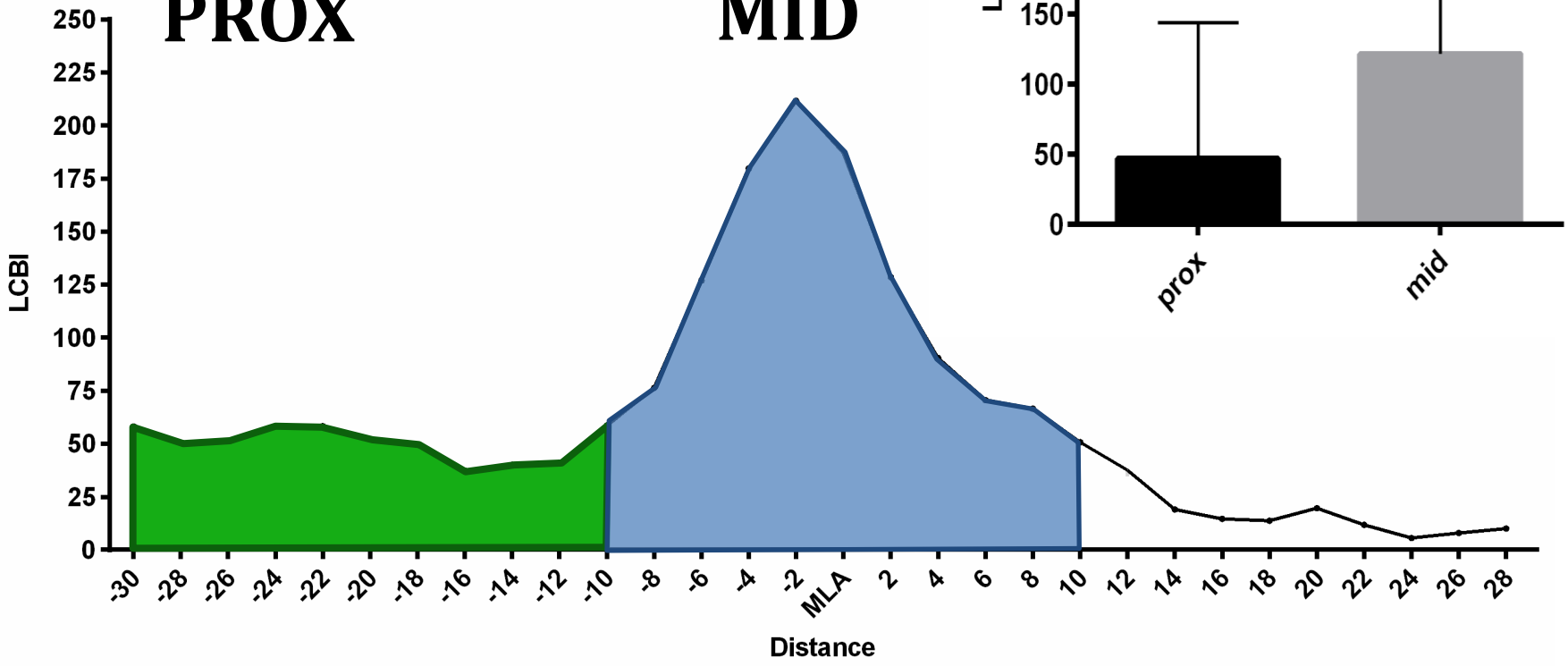


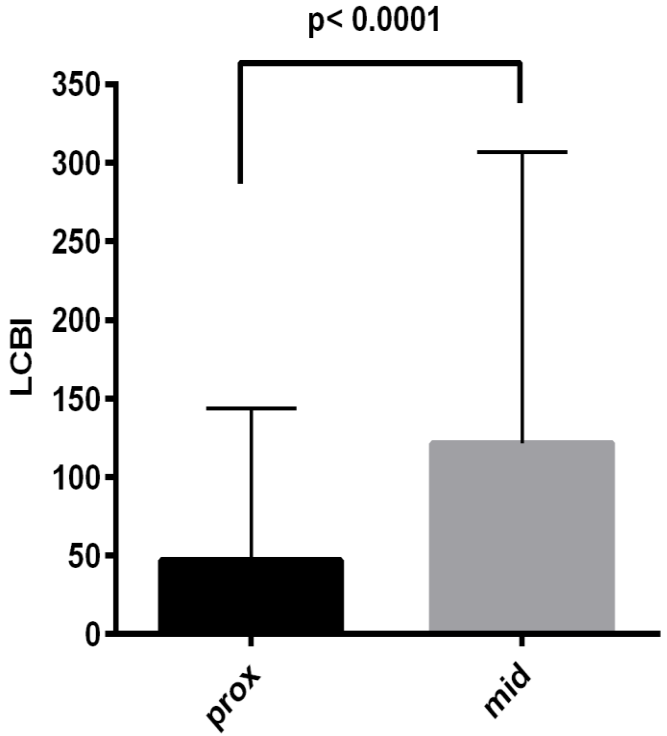
LCBI = 141,5±196,5 vs. 36,11±95,09



Výsledky

LCBI = 141,5±196,5 vs. 54,51±106,3

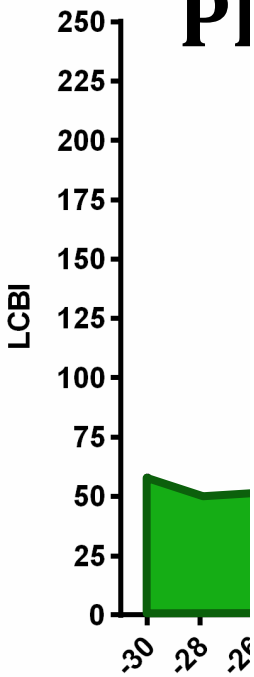


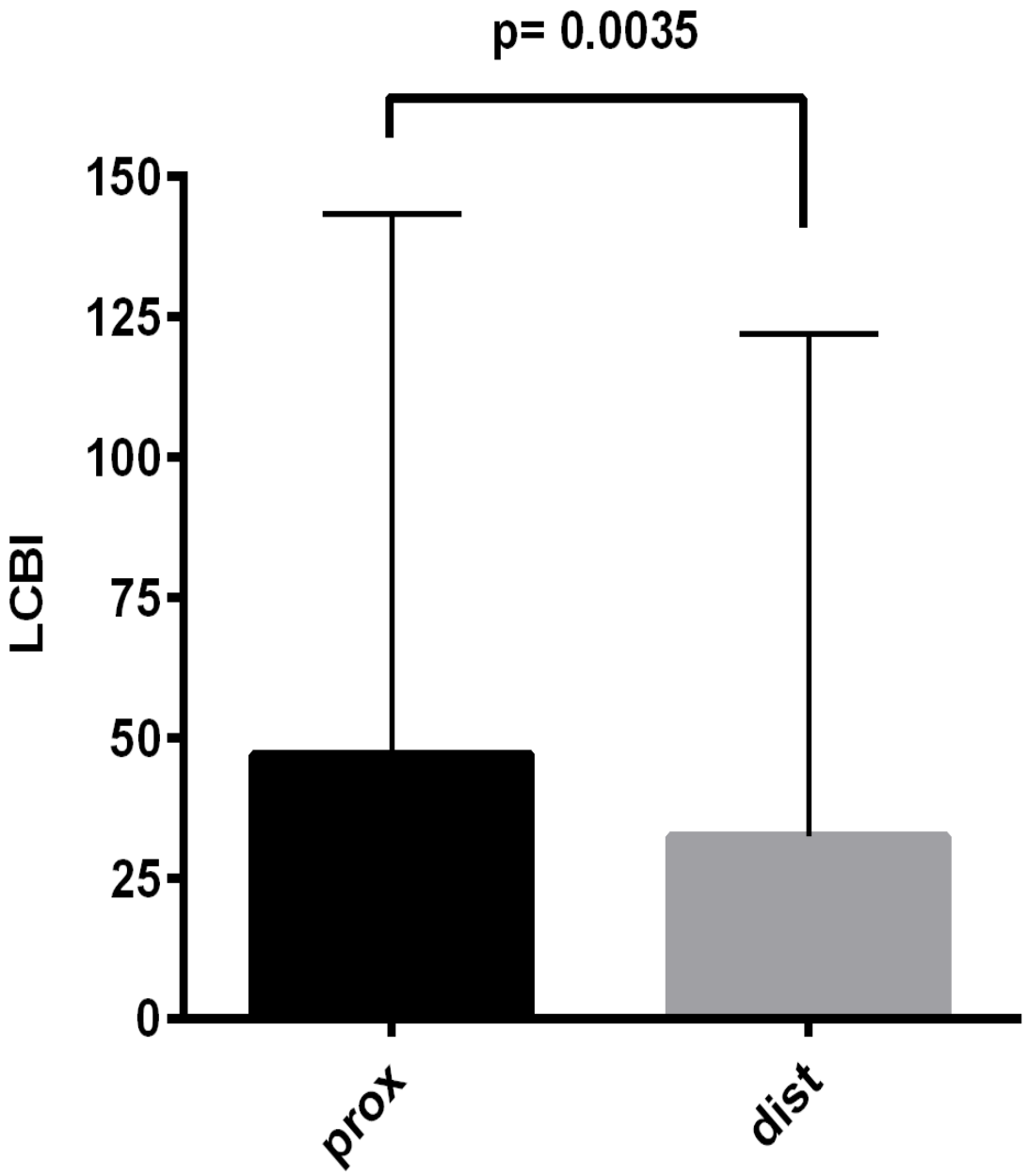


Výsle

LCBI = 54,

Pl **IST**





KLINIKA
TOL

Diskuse

- Naše výsledky naznačují, že se lipidové jádro detekované NIRS vyskytuje častěji v proximálním úseku.
- V literatuře je dobře zavedeno, že proximální část pokročilého karotického plátu je vystavena vysokému ESS.
- Vztah mezi vysokým ESS a projevy destabilizace aterosklerotického plátu byl již dobře popsán zejména ve věnčitých tepnách.
- Data o tomto fenoménu v karotických tepnách jsou dosud omezená.
- Podobná analýza karotického plátu pomocí NIRS doposud nebyla publikována.

Wentzel et al., Eurointervention, 2013
Samady et al., Circulation, 2011
Tuenter et al., Atherosclerosis, 2015
Cheng, et al. Circulation, 2005

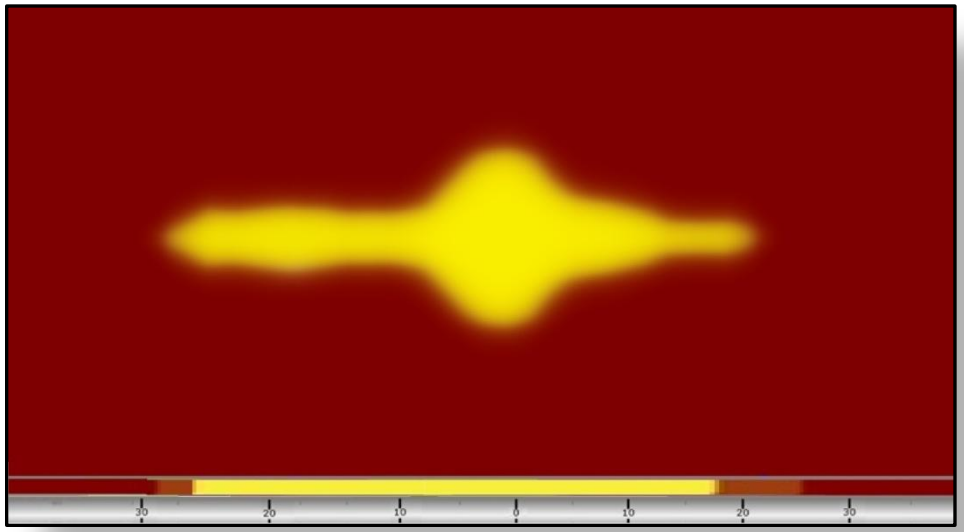
Limitace studie

- Pouze anatomický průkaz výskytu lipidového jádra, vztah k ESS je pravděpodobný, ale mohou hrát roli i jiné faktory

- Asociace lipidového jádra s vulnerabilitou plátu dosud není jednoznačná

Závěr

- Lipidové jádro detekované pomocí NIRS se v rámci pokročilého karotického plátu vyskytuje častěji v jeho proximálním úseku.



FN MOTOL

Děkuji za pozornost