### An overview of safety aspects with blood-flow restricted exercise



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#### Talk outline

- Is it safe to do BFR?
- Which tools can help me assess risk in clinical practice?



From a safety perspective: What is BFR?





An intervention that manipulates blood flow



#### From a safety perspective: What are the concerns?

- 1) Adverse cardiovacular responses
- 2) Blood clotting and vascular function
- 3) Nerve and muscle damage

#### For example



Figure 1. Rudolf Virchow (1821-1902). Courtesy of the National Library of Medicine.

#### Thrombosis risk factors (Virchow's triad)



Kumar et al (2010). Clin Med Res 8: 168-172.

The clinical question that we are trying to answer

#### Is blood-flow restricted exercise safe?



#### Compared to what?



#### Brisbane teen Ben Shaw dies in hospital after weightlifting accident at Pine Rivers PCYC gym

By Kristian Silva and Ashleigh Stevenson Updated 1 Oct 2017, 6:26am



Un-assisted bench press

# Making the question more specific: the PICOT approach

#### **Education reviews**

#### The PICOT criteria

- P Population (patients)
- I Intervention
- C Comparison group
- O Outcome of interest
- T Time

- What patient population are you interested in?
- · What is your investigational intervention?
- What is the main alternative to compare with the intervention?
- What do you intend to accomplish, measure, improve, or affect?
- What is the appropriate follow-up time to assess outcome?



Bandholm et al (2017). Br J Sports Med 51: 1494-1501.

Population

#### Theoretical "at-risk" populations

People with high blood pressure (BP > 160-180/95-100 mmHg)
People with heart disease (e.g. arrhythmia or ischemic)
People with previous thrombo-embolic events (e.g. DVT)
People with a family history of clotting disorders

Intervention

#### Which exercise modality and protocol?

Strength training

Cardiovascular exercise





#### Comparator

#### Strength training (>70% 1RM) most commonly used



#### Outcome





#### **Clinical harms outcome**

Not all will experience one

**Clinically relevant** 

Requires large N's

#### Surrogate harms outcome

Can be measured in all

Association with clinical outcome?

Clinical relevance?

Requires small(er) N's

#### Time frame



#### The search



**Population:** Humans (MeSH) (no population-specific data)

**ntervention:** "Blood-flow restricted exercise" OR ... (synonyms)..

Comparator: N.a. (for a broad search)

Outcome: Patient harm (MeSH) OR Safety (MeSH).... (synonyms)...

**ime frame:** N.a. (for a broad search)





Ideally			The reality		
Question	Level 1	Level 2	Level 3	Level 4	Level 5
What are the <b>COMMON</b> harms?	SR of RCTs	RCT	Cohort	Case-series	Mechanism- based reasoning
What are the <b>RARE</b> harms?	SR of RCTs	RCT	Cohort	Case-series	Mechanism- based reasoning

OCEBM Levels of Evidence Working Group\*. "The Oxford 2011 Levels of Evidence". Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653 \* OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson.

### Surrogate harms outcomes



#### Surrogate harms outcomes (risk population)

Clin Physiol Funct Imaging (2013) 33, pp11-17

doi: 10.1111/j.1475-097X.2012.01

#### Haemostatic and inflammatory responses to blood flow-restricted exercise in patients with ischaemic heart disease: a pilot study

Haruhiko Madarame, Miwa Kurano, Kazuya Fukumura, Taira Fukuda and Toshiaki Nakajima

Department of Ischemic Circulatory Physiology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

"The results suggest that applying BFR during low-intensity resistance exercise does not affect exercise-induced haemostatic and inflammatory responses in stable IHD patients." (N=9)

#### **ORIGINAL ARTICLE**

#### Use and safety of KAATSU training: Results of a national survey

T. Nakajima, M. Kurano, H. Iida, H. Takano, H. Oonuma, T. Morita, K. Meguro, Y. Sato, T. Nagata, and KATTSU Training Group

Int. J. KAATSU Training Res. 2006; 2: 5-13

- 105 KAATSU facilities in Japan (e.g. hospitals and clinics)
- 12,642 persons (20 to 80 yrs) with different conditions
- More than 30,000 BFR exercise sessions
- Most prevalent indication: low muscle strength or atrophy



**Figure 9.** The most frequent side effects of KAATSU training.

(N=12,642, > 30,000 BFR sessions)

Nakajima et al (2006). Int J KAATSU Training Res 2: 5-13.

JOURNAL OF SPORTS SCIENCES, 2018 VOL. 36, NO. 2, 123–130 https://doi.org/10.1080/02640414.2017.1284341





#### The role of blood flow restriction training for applied practitioners: A questionnairebased survey

Stephen D. Patterson (D<sup>a</sup> and Christopher R. Brandner<sup>b</sup>

<sup>a</sup>School of Sport, Health & Applied Science, St Marys University, London, UK; <sup>b</sup>Sport Science Department, Aspire Academy for Sports Excellence, Doha, Qatar

- 250 responders (practitioners) from 20 countries
- 115 of the 250 responders prescribed BFR for different conditions
- Unknown number of BFR participants and exercise sessions
- Most prevalent prescription aim: induce hypertrophy or reduce atrophy

Question: "Do your clients ever report any side effects" (N=99 respondents, N=154 responses)



#### BFR harms outcomes are likely under-reported

Ann Intern Med. 2004;141:781-788.

Improving Patient Care

# Better Reporting of Harms in Randomized Trials: An Extension of the CONSORT Statement

John P.A. Ioannidis, MD; Stephen J.W. Evans, MSc; Peter C. Gøtzsche, MD, DrMedSci; Robert T. O'Neill, PhD; Douglas G. Altman, DSc; Kenneth Schulz, PhD; and David Moher, PhD, for the CONSORT Group\*

"....reporting of harms in RCTs has received less attention than reporting of efficacy and effectiveness and is often inadequate."

# How to risk stratify patients in clinical practice?

#### Why are BFR harm outcomes likely under-reported?

- Focus is efficacy
- No definition consensus on harms
- CONSORT not mandatory for all journals



CONSORT 2010 Key Documents



Reporting of harms better in strength training trials published after 2010

Liu & Latham (2010). Arch Phys Med Rehabil 91: 1471-1473.

Item 19: Harms

#### **Risk stratification tools**

#### No BFR

History of deep vein thrombosis Acute sickness or fever Blood pressure > 180/100 mmHg Early postoperative period Higher class arrhythmia or coronary ischemia	5 points
Pregnancy	4 points
Varicose veins Prolonged inactivity Atrial fibrillation or heart failure Blood pressure160-179/95-99 mmHg	3 points
Age > 60 years, BMI > 30 kg/m², malignancy, hyperlipidemia, oestrogen therapy	2 points
Age 40-58 years, women, BMI 25-30kg/m <sup>2</sup>	1 point

#### Risk stratification tools

MAGNITU- DE OF RISK	MEDICAL HISTORY OR LIFESTYLE FACTOR	PATIENT RESPONSE	DECISION
ABSOLUTE	Do you have a family history of clotting disorders	YES	STOP
	(e.g. SLE (lupus), haemophilia, high platelets)?	NO	CONTINUE
	Do you have level 1 hypertension (SAP $\ge$ 140	YES	STOP
	mmHg)?	NO	CONTINUE
	Do you have a past history of DVT or pulmona-	YES	STOP
	ry embolus?	NO	CONTINUE
	Have you suffered from a haemorrhagic or	YES	STOP
	thrombotic stroke?	NO	CONTINUE
	Do you have level 1 hypertension (SAP ≥ 140 mmHg)? Do you have a past history of DVT or pulmonary embolus? Have you suffered from a haemorrhagic or thrombotic stroke?	YES NO YES NO YES NO	STOP CONTINUE STOP CONTINUE STOP CONTINUE

# SUMMARY

- Use the correct technique and standardized risk assessment (cuff, pressure, exercise dosage/intensity, DVT history, etc.)
- Surrogate harms outcomes indicate BFR to influence cardiovascular, nerve, and muscle function comparable to highintensity strength training (level 5 evidence).
- Common clinical harms include: DOMS, subcutaneous hemorrhage, and numbness (level 4 and 5 evidence).
- Rare (serious) clinical harms include: rhabdomyolysis and venous thrombosis (level 4 and 5 evidence).
- BFR harms outcomes are very likely under-reported in the literature.



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#### "How to" ressources

#### The Application of Blood Flow Restriction: Lessons From the Laboratory

Kevin T. Mattocks<sup>1</sup>; Matthew B. Jessee<sup>1</sup>; J. Grant Mouser<sup>1</sup>; Scott J. Dankel<sup>1</sup>; Samuel L. Buckner<sup>1</sup>; Zachary W. Bell<sup>1</sup>; Johnny G. Owens<sup>2</sup>; Takashi Abe<sup>1</sup>; and Jeremy P. Loenneke, PhD<sup>1</sup>

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WORKSHOP // This workshop is an extension of the symposium 'Blood flow restricted exercise after surgery or disease: Adaptations, clinical efficacy and safety'. This new and promising training modality will be demonstrated and practiced.

Friday 9.55 a.m., Room "Jylland"

# Thank you

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#### The way forward: "Post-marketing" safety studies

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2008; 17: 1226–1234 Published online 27 October 2008 in Wiley InterScience (www.interscience.wiley.com) DOI: 10.1002/pds.1675

#### ORIGINAL REPORT

### A distributed research network model for post-marketing safety studies: the Meningococcal Vaccine Study $^{\dagger}$

Priscilla Velentgas PhD<sup>1\*</sup>, Rhonda L. Bohn ScD, MPH, FISPE<sup>2</sup>, Jeffrey S. Brown PhD<sup>1</sup>, K. Arnold Chan MD, ScD, FISPE<sup>3,4</sup>, Patricia Gladowski RN, MS<sup>5</sup>, Crystal N. Holick ScD, MPH<sup>4</sup>, Judith M. Kramer MD, MS<sup>6</sup>, Cynthia Nakasato MD<sup>7</sup>, Claire M. Spettell PhD<sup>8</sup>, Alexander M. Walker MD, DrPH, FISPE<sup>3,9</sup>, Fang Zhang PhD<sup>1</sup> and Richard Platt MD, MPH<sup>1</sup>