

## СПАСЕН ВИТАЛЕН ХИБЕРНИРАЩ МИОКАРД СЛЕД ПТКА. ПРОМЯНА НА ВКЛЮЧВАНЕТО НА Tl-201 В ДИСИНЕРГИЧНАТА ОБЛАСТ

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## SALVAGE OF VIABLE HYBERNATING MYOCARDIUM AFTER PTCA. THALLIUM UPTAKE CHANGES IN THE ASYNERGIC SEGMENTS

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Посредством СПЕКТ-миокардна перфузионна сцинтиграфия и контрастна вентрикулография се определят промените в перфузията и функционалното състояние на лявата камера при 8 пациента с 11 хронични оклузии на коронарните артерии, настъпващи в двумесечен срок от ПТКА. Преди ПТКА чрез рест-преразпределителната техника се уточнява наличието на витален хиберниращ миокард в дисинергичните участъци. От общо 30 сегмента, свързани с дисинергии, 14 са с хипокинезия, 11 - с акинезия, 5 - с дискинезия. 20 от тях са с данни за витален, хиберниращ миокард. Така се представят всички хипокинетични и 6 от акинетичните сегменти. Промени във включването на Tl-201, респ. на перфузията след ПТКА, се установяват при 15 от тях, като останалите 5 са свързани с наличие на ранни или късни усложнения на процедурата (на практика без реперфузия). Промяната в кинетиката на дисинергичните сегменти след ПТКА се изразява в нормализиране на кинетиката на 6 от хипокинетичните и подобрене на кинетиката на 6 от акинетичните сегменти, с което се променя общият брой на дисинергичните участъци и вида на кинетичните нарушения. Подобрието в общата фракция на изтласкване (средно с  $8.8\% \pm 5.6\%$ ) е по-изразено при преобладаване на хипокинетичните сегменти в територията на оклузията, но се среща и може да е значително и при наличие на акинетични сегменти с витален хиберниращ миокард. Рест-преразпределителната миокардна перфузионна сцинтиграфия с Tl-201 определя коректно сегментите с хиберниращ миокард и може да служи за прогнозиране на функционалното подобрене. Проведеното изследване потвърждава приложимостта и функционалното отражение на ПТКА при хронични оклузии, пряко свързано с прогнозата.

In 8 patients with 11 chronic occlusions the changes in the myocardial perfusion and left ventricular function were determined before and 2 months after PTCA by SPECT perfusion scintigraphy and contrast ventriculography. The presence of the viable hibernating myocardium was evaluated before PTCA in the asynergic segments by rest-redistribution technique. Out of 30 segments with kinetic abnormalities 14 were hypokinetic, 5 - dysketic and 11 - akinetic. 20 segments (67%) showed a presence of viable myocardium, including all of the hypokinetic and 6 from the akinetic segments. In 15 of those segment with wall motion changes we also found alterations in the Tl-201 uptake after PTCA. The 5 resting segments were related to early or late complications as a result of revascularization and remained without any reperfusion. The kinetic changes after PTCA consisted in normalization in 6 of the hypokinetic segments and improvement with 1 degree in 6 of the akinetic segments. Thus the total number of segments with dyssinergy decreased including mainly the segment number presented before the procedure with severe abnormalities. The improvement in the left ventricular ejection fraction ( $x = 8.8\% \pm 5.6\%$ ) depended on the degree of the kinetic abnormalities. the kinetic improvement was remarkable after reperfusion of hypokinetic regions, but this trend also appeared in the akinetic regions with viable hibernating myocardium. The study confirmed the beneficial effect of PTCA on the left ventricular function in pts with chronic occlusion as being directly related to the prognosis. The rest-redistribution Tl-201 myocardial perfusion scintigraphy correctly determined the hibernating myocardium and predicted the benefit of the procedure.

**Key words:** angioplasty, transluminal, percutaneous coronary; myocardial reperfusion; coronary disease/surgery; ventricular function, left

# Перкутанна транслуминална ангиопластика при пациенти с хронично оклудирани коронарни съдове - първичен успех и остри усложнения

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## Резюме

Коронарната транслуминална ангиопластика при хронични коронарни оклузии се свързва с по-нисък първоначален успех. За да определим първоначалния успех и оценим възможните клинични и ангиографски показатели, свързани с първоначалния успех и острите усложнения, ние изследвахме 84 пациенти с хронична коронарна оклузия, преминали през Клиниката по кардиология към УБ „Св.Екатерина“ за периода от януари 1991 г. до юни 1995 г. 64 от пациентите (76.2%) са мъже, и 20 (23.8%) са жени, при средна възраст общо  $53 \pm 10$  години.

Първичен ангиографски успех бе постигнат при 67 болни (79.76%).

От анализираният показатели, статистически значими за постигане на успех се оказаха следните фактори: функционална оклузия, източен край на съда на мястото на оклузията, по-голям диаметър на дилатирания съд. От друга страна давността на оклузията, наличието на свързващи (bridging) колатерали, по-малкият диаметър на съда и тоталната оклузия са фактори, предполагащи неуспех.

Нито един от изследваните фактори нямаше отношение към острите усложнения. От тежките усложнения само при един пациент (1.19%) се наложи операция по спешност.

Изводи: ПТКА е метод, който може да се използва за лечение на пациенти с хронично оклудирани коронарни съдове със задоволителен резултат и нисък очакван риск.

**Ключови думи:** хронична коронарна оклузия, лечение, ПТКА

## Summary

### Percutaneous transluminal coronary angioplasty of chronic occlusion: primary success and acute complications

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Percutaneous Transluminal Coronary Angioplasty (PTCA) of chronic total occlusion is known to be with a lower success rate than angioplasty for stenotic lesions. In this study our aim was to determine the success rate and assess clinical and angioplastic variables associated with success and complications.

We analysed the results of PTCA for chronic occlusion in 84 patients, performed in the Cardiology Clinic of „St. Ekaterina“ University Hospital from January 1991 to June 1995. 64 (67.86%) of our patients were men and 20 (23.80%) women. The average age was  $53 \pm 10$ . All patients were with clinical duration of the occlusion of more than one month. 57 (67.86%) of them were with total occlusions, and 27 (32.14%) - functional. Most of the patients were with angina class III - 45 (53.57%) by the Canadian classification and 28 (33.33%) - class IV.

45 patients (53.57%) were with single vessel disease and 39 (46.43%) were with multivessel disease. 17 patients (20.24%) were with left ventricular ejection fraction of less than 35%.

Primary success was achieved in 67 (79.76%) patients.

Success rate in patients with total occlusion was 75.44% and with functional 88.89%.

The statistically significant predictors of success were functional occlusion, tapered end of the occlusion and larger diameter of the vessel. Bridging collateral, duration of occlusion and abrupt morphology at the point of the occlusion, as well as smaller diameter of the vessel were found to be very strong predictors of failure.

Major acute complications were very rare - only 1 (1.19%) patients had to have an urgent CABG. No clinical or angiographic variables had any impact on the complications rate.

Conclusions: PTCA can be used as a revascularisation method with a satisfactory success rate and a very low risk of major complications.

**Key words:** chronic coronary occlusion, treatment, PTCA

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## Оценка на пациенти с исхемична болест на сърцето и левокамерна дисфункция чрез вариабилност на сърдечната честота и късни потенциали

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Изследвани са общо 40 болни с исхемична болест на сърцето (ИБС), разделени на две групи: I група - 20 болни с дисфункция на лявата камера (ЛК) и II група - 20 болни без дисфункция на ЛК. При всички болни функцията на ЛК е оценена ехокардиографски и/или ангиокардиографски. Компютърната обработка на електрокардиографските записи е извършена с апарат на фирмата „Шилер“. Самостоятелно са определени показателите за вариабилност на сърдечната честота и късни потенциали. Направен е опит за оценка на необходимостта от изследване поотделно или заедно на вариабилността на сърдечната честота и на късните потенциали с оглед прогнозата при болните с ИБС и левокамерна дисфункция.

## TI-201 СПЕКТ за диагностика на витален миокард при хронични оклузии

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Целта на проучването е да се определи наличието и количеството витален миокард при хронични оклузии като предиктор на функционалното подобрение след реканализация на съда. Изследвани са 8 болни (7 мъже и 1 жена от 38 до 65г.) с оклузия на коронарен съд с давност от 2 до 14 месеца и значителни кинетични нарушения на съответстващия участък от левокамерната стена. СПЕКТ-миокардната перфузионна сцинтиграфия се извършва по рест-преразпределителна техника. Сегментите, свързани с оклудирания съд се оценяват количествено, като включването на TI-201 се представя в процент от максималното за съответния срез. Кинетичните нарушения се оценяват като хипо или а/дискинетични.

Установява се, че всички сегменти с адискинезия имат включване на TI-201  $\leq 53\%$ , а тези с хипокинезия  $\geq 60\%$ . Като витални се определят последните, както и тези с подобрение на включването на 4 час с  $\geq 10\%$ . От 52 сегмента, свързани с оклудирания съд, данни за витален миокард има при 35-67%. Съотношението витални/невитални сегменти е незначимо по-високо при давност на оклузията  $\leq 6$  месеца - 18/7, отколкото при давност  $> 6$  месеца - 17/10. Има значима разлика в съответствието витални/невитални сегменти при наличие и липса на колатерално кръвообращение. Липсата на колатерали обаче не предсказва липса на витален миокард.

## Тайм-дилей в началото на сегментната контракция като степен на хиберниран миокард

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Изследвани са 30 болни с Исхемична болест на сърцето /ИБС/ (ср.възраст  $56.7 \pm 7.4$ ), без миокарден инфаркт, от които 20 са със сигнификантна едноклонова лезия, а 10 с тотална оклузия на един коронарен съд. Определена е сегментната функция на левокамерния миокард като скъсяване /"Шортенинг"/ и закъсняване на контракцията /"Тайм дилей"/. Същите показатели са изследвани и след прилагане сублингвално на нитроглицерин. Като база за сравнение са стойностите от 20 пациента с нормална коронарна морфология. Отчита се доминираща абнормност за определени сегменти: антеролатерален, апикален и постеробазален - с шортенинг, а при антеробазалния и диафрагмален - съотв. с Тайм дилей. Като независим показател Тайм-дилей се изявява самостоятелно в 18% от изследваните сегменти, а заедно със сегментното скъсяване /Шортенинг/ увеличава сегментната абнормност от 22% до 40%.

Редуцирането на абнормните сегменти, като абсолютен брой и процент, след прилагането на нитроглицерин демонстрира, че "Шортенинг" и "Тайм дилей" са изява на миокардна хибернация, като последната форма е и със своето самостоятелно значение, отразяващо функционалното състояние на левокамерния миокард в условията на хронична коронарна недостатъчност.

## Диастолната асинхронност - независима детерминанта на промените в бързото пълнене на исхемична лява камера със запазена систолна функция

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## Секция „Интервенционална кардиология“

### PTCA - надежден метод за реваскуларизация в първите часове на острия миокарден инфаркт и средство на избор при кардиогенен шок

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Големината на загубената мускулна маса оказва огромно значение върху близката и далечната прогноза, при болен с остър миокарден инфаркт (ОМИ). Ранното и сигурно отваряне на оклудирания коронарна артерия, ограничаването на миокардната исхемия и съхраняването на левокамерната (ЛК) функция е основен проблем на съвременната кардиология.

В настоящото проучване се анализират резултатите от PTCA извършена в първите часове на МИ и при болни в кардиогенен шок, в ИБ „Св. Екатерина“ - София, за периода от 1993 - 1996 год.

**МАТЕРИАЛ И МЕТОДИ:** Изследвани са общо 22 болни, разделени в две групи - ОМИ и кардиогенен шок. При всички е проведена PTCA, като при една част от случаите с ОМИ - първична PTCA (до шестия час от началото на МИ с или без фибринолиза). Пациентите са проследявани за появата на ранни (ранна смъртност, ре-инфаркт, коронарен байпас по спешност) и късни усложнения ( рецидив на АП, повторен МИ, планова САВГ хирургия, ре-PTCA и късна смъртност) за период от 6 до 12 месеца.

**РЕЗУЛТАТИ:** При проследяването на пациентите в групата с ОМИ - ранни усложнения не се наблюдаваха. Късни усложнения - повторен миокарден инфаркт се наблюдава при един пациент (4,5 %) с многоклонова коронарна болест, завършил летално и планова САВГ хирургия при един пациент (4,5 %) с многоклонова коронарна болест. В групата на болните с кардиогенен шок - ранни усложнения - спешен САВГ при двама пациенти с многоклонова коронарна болест. Късни усложнения не се наблюдаваха.

**ИЗВОД:** PTCA е надежден метод за реваскуларизация в първите часове на ОМИ и средство на избор при кардиогенен шок.

### Обобщени резултати от провеждането на транслуминална коронарна ангиопластика при пациенти с нестабилна ангина пекторис в УБ „Св. Екатерина“ за периода 1991 - февруари 1996

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**Материали и методи:** След въвеждането на PTCA, тя се превърна в основен метод за лечение на НАП, неподдаваща се на медикаментозно лечение. Направи се анализ на резултатите от PTCA при 54 пациенти с НАП от 1991 г. до февруари 1996 г.

Пациентите са групирани според:

1. Новопоявила се или акцелерираща АП
2. Стенокардия в покой с ЕКГ промени
3. Ранна постинфарктна стенокардия

Сформират се 2 основни групи:

1. Първично стабилизирана НАП - с отложена спешност
2. Рефрактерна на медикаментозна терапия НАП - по спешност

Пациентите бяха наблюдавани за:

А/ Ранни усложнения

- а/ смъртност
- б/ миокарден инфаркт
- в/ САВГ - по спешност

Б/ Късни усложнения

- а/ рецидив на стенокардията
- б/ МИ
- в/ планов САВГ
- г/ ге - PTCA
- д/ късна смъртност

Период на наблюдение 6 - 12 месеца.

**Резултати**

**1 гр. 39 пациенти 72,2%**

А. Ранни усложнения: ранна смъртност **0%**; остър МИ **5,1%**; САВГ по спешност **2,6%**

Б. Късни усложнения: рецидив на стенокардията **23,1%**; МИ **2,6%**; късна смъртност **2,6%**; САВГ **7,7%**;

# Обобщени резултати от перкутанна транслуминална коронарна ангиопластика в ДИБ „Света Екатерина“ за периода 1991 – 1994 година

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## Summent up Results Percutaneous Transluminal Coronary Angioplasty According to the Case Material of the St. Catherine Hospital, Covering the Period 1991-1994

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### Резюме

Прави се анализ на резултатите от PTCA при 164 пациенти в ДИБ "Света Екатерина" за периода януари 1991 - април 1994 г.

Пациентите бяха разделени в четири групи:

- I. Стабилни стенокардия.
- II. Нестабилна стенокардия:
  - a) първично стабилизирана;
  - b) рефрактерна към лечение.
- III. Остър миокарден инфаркт (ОМИ).
- IV. Тиха исхемия.

Пациентите са били наблюдавани за появата на:

- A) Ранни усложнения:
  - a) смъртност; б) миокарден инфаркт (МИ); в) коронарен байпас по спешност;
- Б) Късни усложнения:
  - a) рецидив на стенокардията; б) миокарден инфаркт;
  - в) нужда от коронарен байпас; г) re-PTCA; д) късна смъртност.

Периодът на наблюдение беше от 6 до 12 месеца.

Резултати:

I група - 1) ранни усложнения - ранна смъртност - 0 %; остър МИ - 0 %; CABG по спешност - 5 %; 2) късни усложнения - рецидив на стенокардията - 8,4 %; МИ - 1,5 %; късна смъртност - 0 %; изборителна CABG - 0,8 %; re-PTCA - 6,5 %.

II група - 1) ранни усложнения - ранна смъртност - 0 %; остър МИ - 6 %; спешна CABG - 3 %; 2) късни усложнения - късна смъртност - 6 %, рецидив на стенокардията - 10 %; МИ - 6 %; изборителна PTCA - 14 %.

III група - 1) ранни усложнения - ранна смъртност - 0 %; остър МИ - 17 %; спешна CABG - 17 %; 2) късни усложнения - рецидив на стенокардията - 17 %, МИ - 17 %; късна смъртност - 17 %, изборителна CABG - 0 %, re-PTCA - 0 %.

IV група - 1) ранни усложнения - ранна смъртност - 0 %, остър МИ - 0 %; спешна CABG - 0 %, рецидив на стенокардията - 18 %, късен МИ - 0 %, късна смъртност - 0 %, изборителна CABG - 0 %, re-PTCA - 18 %.

PTCA е безопасен и надежден метод за реваскуларизация не само при пациенти със стабилна стенокардия, но също така и при болни с остри коронарни синдроми.

Ключови думи: PTCA, СТАБИЛНА СТЕНОКАРДИЯ, НЕСТАБИЛНА СТЕНОКАРДИЯ, ОСТЪР МИ

### Summary

Objectives: The article reviews the results of PTCA in 164 patients in Hospital „St Ekaterina“ in the period January 1994 - April 1994.

Methods: Patients were divided in four groups:

- I Stable angina
- II Unstable angina
  - a) primary stabilized
  - b) refractory to medical treatment
- III Acute myocardial infarction (AMI)
- IV Silent ischaemia

Patients were followed for:

- 1.) Acute complications
  - a) mortality
  - b) myocardial infarction (MI)
  - c) emergency CABG
- 2.) Late complications
  - a) recurrent angina
  - b) MI
  - c) elective CABG
  - d) re-PTCA
  - e) late mortality

Follow-up period was 6-12 months

Results: I group 1) acute complications - early mortality - 0 %; acute MI - 0 %; emergency CABG - 5 %; 2) Late complications-recurrent angina - 8.4 %; MI - 1.5 %; late mortality - 0 %; elective CABG - 0 %; re-PTCA - 6.5 %.

II group 1) acute complications - early mortality - 0 %; acute MI - 6 %; emergency CABG - 3 %; 2) Late complications-late mortality - 6 %; recurrent angina - 10 %; MI - 6 %; elective CABG - 11 %; re-PTCA - 14 %.

III group 1) acute complications - early mortality - 0 %; acute MI - 17 %; emergency CABG - 17 %; 2) Late complications-recurrent angina - 17 %; MI - 17 %; late mortality - 17 %; elective CABG - 0 %; re-PTCA - 0 %.

IV group 1) acute complications - early mortality - 0 %; acute MI - 0 %; emergency CABG - 0 %; 2) recurrent angina - 18 %; late MI - 0 %; late mortality - 0 %; elective CABG - 0 %; re-PTCA - 18 %.

Conclusions: PTCA is a safe and reliable method for revascularization not only in patients with stable angina, but also in patients with acute coronary syndroms.

Key Words: PTCA, STABLE ANGINA, UNSTABLE ANGINA, ACUTE MI

re-PTCA 13,4%

2 гр. 15 пациенти 27,8%

А. Ранни усложнения; ранна смъртност 0%; спешен САВГ 0%; остър МИ 6,7%.

Б. Късни усложнения; рецидив на стенокардията 40%; МИ 13,3%; късна смъртност 6,7%; САВГ 13,3%; re-PTCA 20%

**Изводи:** Независимо от повишения риск от ранни усложнения, PTCA при НАП, се прилага с добър резултат и нисък процент на усложнения. Методът е безопасен и надежден, алтернатива на оперативната реваскуларизация и се прилага при всички пациенти с НАП, чиято коронарна анатомия позволява, и вод до значителен успех по отношение на ранната смъртност 2,1% и МИ 6,1%.

### Продължителна инфлация на автоперфузионен балон-катетър за лечение на острата оклузия на съда след PTCA, приложена в УБ „Света Екатерина“ за периода декември 1994 - февруари 1996 г

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Въпреки успешните ангиопластики, процентът на ранните усложнения все още е висок. По литературни данни 3 до 5% /средно 4,2%/ е остро запущване на съда, предизвикано от тромбоза или дисекация, като поведението е повторна ангиопластика, продължително раздуване на стандартен или автоперфузионен катетър, водещо в повечето случаи до добър резултат. При неуспех може да се използва интракоронарен стент или лазерна балонна ангиопластика. В повечето случаи обичайните дилатационни балони предизвикват ендотелно разкъсване, интимални фисури, чиято пенетрация към медията предизвиква локализирано разслояване на стената на съда и съответно дисекиращ флеп или интрамурален хематом. Към този процес се включва коронарния вазоспазм, активирането на тромбоцитите, водещи до образуването на обтуриращ тромб или стаза на кръвта от дисецирания флеп.

**МАТЕРИАЛИ И МЕТОДИКА:** По литературни данни автоперфузионните катетри позволяват инфлация различна продължителност без данни за миокардна исхемия /клинични, ЕКГ, ензимни/ съответно от 3 минути до 5 часа. В тази статия са описания 6 случая с раздуване на автоперфузионния катетър /АПК/ повече от 60 мин., максимално 24 часа.

Пациентите са проследени за:

1. Ранна смъртност
2. Re-МИ
3. Спешен АСВ
4. Влошаване на ЛК-функция
5. Ранна re-тромбоза

Период за проследяване- 24 часа до 3 месеца.

1. Ранна смъртност - 0%
2. Re-МИ - 13,33% /един случай/
3. Спешен АСВ - 13,33% /един случай/
4. Влошаване на ЛК- функция - 0%
5. Ранна re-тромбоза - 13,33% /един случай, непосредствено след фибринолиза/

По време на инфлацията на АПК, пациентите са наблюдавани за прояви на ангина пекторис - ЕКГ-промени, ензимна динамика, клиника.

**ИЗВОДИ:** Автоперфузионната ангиопластика с продължителност повече от 60 минути се явява алтернативен метод за овладяване на острата коронарна оклузия по време на PTCA, тъй като чрез пасивното преминване на кръвния ток през централния лумен на катетъра, дисталната част на коронарния съд се перфузира адекватно. Методът води до значително намаляване процента на ранните усложнения след остро запущване на съда: смърт, ОМИ и спешен аорто-коронарен байпас.

### Коронарна ангиопластика при болни със силно ограничена левокамерна функция и тежка трисъдова болест

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Рискът при коронарна ангиопластика (ПТКА) на големите съдове при болни с многосъдова болест и силно ограничена левокамерна (ЛК) функция се оценява като висок.

Обект на проучването са 33 болни (27 мъже и 6 жени) на средна възраст  $63,9 \pm 10,95$  год., със силно ограничена ЛК функция (ИФ - 40%) и трисъдова болест, при които в периода 1994-1995 год. е извършена ПТКА. 32 са с преживян миокарден инфаркт, 18 са с прояви на сърдечна недостатъчност - II-IV ФК по НИХА. 26 болни са със стенокардна симптоматика, като 12 са с нестабилна стенокардия IIB и 3 - IIC клас

## Секция „Интервенционална кардиология“

### PTCA - надежден метод за реваскуларизация в първите часове на острия миокарден инфаркт и средство на избор при кардиогенен шок

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Големината на загубената мускулна маса оказва огромно значение върху близката и далечната прогноза, при болен с остър миокарден инфаркт (ОМИ). Ранното и сигурно отваряне на оклудирания коронарна артерия, ограничаването на миокардната исхемия и съхраняването на левокамерната (ЛК) функция е основен проблем на съвременната кардиология.

В настоящото проучване се анализират резултатите от PTCA извършена в първите часове на МИ и при болни в кардиогенен шок, в ИБ „Св. Екатерина“ - София, за периода от 1993 - 1996 год.

**МАТЕРИАЛ И МЕТОДИ:** Изследвани са общо 22 болни, разделени в две групи - ОМИ и кардиогенен шок. При всички е проведена PTCA, като при една част от случаите с ОМИ - първична PTCA (до шестия час от началото на МИ с или без фибринолиза). Пациентите са проследявани за появата на ранни (ранна смъртност, ре-инфаркт, коронарен байпас по спешност) и късни усложнения ( рецидив на АП, повторен МИ, планова САВГ хирургия, ре-PTCA и късна смъртност) за период от 6 до 12 месеца.

**РЕЗУЛТАТИ:** При проследяването на пациентите в групата с ОМИ - ранни усложнения не се наблюдаваха. Късни усложнения - повторен миокарден инфаркт се наблюдава при един пациент (4,5 %) с многоклонова коронарна болест, завършил летално и планова САВГ хирургия при един пациент (4,5 %) с многоклонова коронарна болест. В групата на болните с кардиогенен шок - ранни усложнения - спешен САВГ при двама пациенти с многоклонова коронарна болест. Късни усложнения не се наблюдаваха.

**ИЗВОД:** PTCA е надежден метод за реваскуларизация в първите часове на ОМИ и средство на избор при кардиогенен шок.

### Обобщени резултати от провеждането на транслуминална коронарна ангиопластика при пациенти с нестабилна ангина пекторис в УБ „Св. Екатерина“ за периода 1991 - февруари 1996

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**Материали и методи:** След въвеждането на PTCA, тя се превърна в основен метод за лечение на НАП, неподдаваща се на медикаментозно лечение. Направи се анализ на резултатите от PTCA при 54 пациенти с НАП от 1991 г. до февруари 1996 г.

Пациентите са групирани според:

1. Новопоявила се или акцелерираща АП
2. Стенокардия в покой с ЕКГ промени
3. Ранна постинфарктна стенокардия

Сформират се 2 основни групи:

1. Първично стабилизирана НАП - с отложена спешност
2. Рефрактерна на медикаментозна терапия НАП - по спешност

Пациентите бяха наблюдавани за:

А/ Ранни усложнения

- а/ смъртност
- б/ миокарден инфаркт
- в/ САВГ - по спешност

Б/ Късни усложнения

- а/ рецидив на стенокардията
- б/ МИ
- в/ планов САВГ
- г/ ге - PTCA
- д/ късна смъртност

Период на наблюдение 6 - 12 месеца.

**Резултати**

**1 гр. 39 пациенти 72,2%**

А. Ранни усложнения: ранна смъртност **0%**; остър МИ **5,1%**; САВГ по спешност **2,6%**

Б. Късни усложнения: рецидив на стенокардията **23,1%**; МИ **2,6%**; късна смъртност **2,6%**; САВГ **7,7%**;

# Анатомични особености на а. mammaria Interna и значението им за оперативните резултати при аорто-коронарен байпас

(Съобщение за 2 клинични случая с големи интеркостални клонове на а. mammaria interna)

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## Anatomical Patterns of A. Mammaria Interna and Their Impact on the Operative Outcome of Aortocoronary Bypass

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### Резюме

Това проучване прави опит за определяне на възможността от поява на синдром на обкраждане след коронарни операции, при които вътрешната мамарна артерия (ИМА) е използвана като трансплантант, без лигиране на нейните големи странични клонове.

Вътрешната мамарна артерия (ИМА) се смята за кръвоносен съд от първи избор за извършването на коронарен байпас. (CABG). Все по-често се използват трансплантанти от ИМА, все повече нараства значението на аномалиите на ИМА и особено на големите клонове върху постоперативните резултати. Известно е значението на коронарния подклучичен синдром на обкраждане.

Представяме два клинични случая с големи интеркостални клонове, визуализирани посредством постоперативна коронарна ангиография, проведена с оглед оценка на състоянието на коронарните и трансплантираните съдове по повод на рецидивна постоперативна стенокардна болка. След сърдечната катетризация проведохме ЕКГ стрес-тестове в следната последователност: 1. Конвенционален стрес-тест на тредмил (за контрола) и 2. Модифициран стрес-тест, натоварващ мускулите на гръдната стена в положение на гръб. Надявахме се да провокираме и след това да оценим феномена на обкраждане от главния клон на ИМА към големите латерални клонове. И при двамата пациенти при ангиографията се визуализираха трансплантантите на ИМА, като и двата имаха необикновено широки (> 50 % от лумена ИМА) странични клонове, намаляващи кръвния поток в ИМА-трансплантанта. Модифицираният стрес-тест с натоварване на мускулите на гръдната стена не провокира ангинална болка и при двамата пациенти. При единия от тях (50-годишна бяла жена, CABG x 3 - юли 1993) се наблюдаваше незначителна ST-депресия (< 2 mm) във V<sub>4</sub> - V<sub>5</sub> (съмнение за "тиха" исхемия). При другия пациент (70-годишен бял мъж, преден МИ - 1990, CABG x 4 - 1992) стрес-тестът беше прекъснат поради умора в ръката. Не се наблюдаваха съществени промени в ЕКГ.

Въпреки че не можахме да докажем феномена на обкраждане чрез ангиографското изследване и модифицирания ЕКГ стрес-тест, ние бихме могли да направим няколко логични заключения.

### Summary

Objectives: This study attempted to determine the possibility for steal phenomenon after coronary surgery using Internal Mammary Artery (IMA) as graft with unligated big side branches.

The Internal Mammary Artery (IMA) is considered to be the conduct of choice in Coronary Artery Bypass Grafting (CABG). The more IMA grafts are used, the more increases the significance of IMA anomalies and notably the large side branches for the surgical results. The importance of coronary subclavian steal syndrome is well known.

We represent two clinical cases with big intercostal branches visualised at the postoperative coronary angiography, performed to evaluate the coronary and graft status cause of recurrent postoperative anginal pain. After cardiac catheterization we performed ECG stress test as follows: 1. A conventional stress test on Treadmill (for control) and 2. Modified stress test loading the chest wall muscles in spine position. We expected to provoke and to evaluate steal phenomenon by the main IMA graft to the big lateral branches.

At both of the patients on the arteriographic study IMA graft was patent and both had unusual large (> 50 % of the IMA lumen) side branches, reducing the blood flow in the IMA graft. The modified stress test loading the chest wall muscles didn't provoke anginal pain at both patients. At the first (50 years old white male, CABG x 3 - July 1993) it was evident non significant ST depression (< 2 mm) in V<sub>4</sub> - V<sub>5</sub> (suspension of silent ischemia). At the second (70 years old white male, anterior MI-1990, CABG x 4 - 1992) the stress test was interrupted because of fatigue at the arm. No evident significant ECG changes.

Despite we couldn't prove steal phenomenon through the angiographic study and the modified ECG stress test we suggest several logic.



REVIEW

## NON-PHARMACOLOGICAL METHODS IN THE TREATMENT OF RESISTANT HYPERTENSION

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### ABSTRACT

**INTRODUCTION:** Arterial hypertension is the most common chronic cardiovascular disease affecting about 25% of the adult population. Meta-analyses have demonstrated a linear relationship between blood pressure and the risk of cardiovascular events. Resistant hypertension defined as failure to reach blood pressure targets despite treatment with three antihypertensive drugs including a diuretic represents a serious clinical problem. It has been estimated that it affects between 8.9% and 12.8% of all treated hypertensive subjects. In resistant hypertension the optimal blood pressure is illusive despite very well tailored therapy.

**OBJECTIVE:** Management of resistant hypertension is exactly the field where blood pressure-controlling non-pharmacological methods fit best. The present article aims at throwing light on these methods' principles of action, on who the target patient groups are and the respective results. Two methods are especially reviewed here: the carotid baroreflex stimulation and the transcatheter renal sympathetic denervation.

Current results from the use of renal denervation suggest stable efficiency of the method, the results becoming significant 6 months after the procedure is applied and sustained for two years in the follow-up. As much as 90% of the treated patients respond to the procedure. The transcatheter renal denervation is associated with only 2.61% of procedural complications. The baroreflex carotid stimulation, too, is known to produce a stable effect on blood pressure: the effect become obvious at 12 months in 88% of the treated subjects. The neurologic complications associated with the procedure are reported to occur in 4.4% of cases.

**CONCLUSION:** The present review article clearly demonstrates that non-pharmacological methods for treatment of resistant hypertension show great promise despite some open questions concerning their long term effects and procedural safety.

**Key words:** resistant hypertension, renal denervation, baroreflex stimulation

### INTRODUCTION

Arterial hypertension (AH) is the most common chronic disease in modern societies, affecting about 25% of the adult population.<sup>1</sup> Meta-analyses have demonstrated a linear correlation between the levels of blood pressure (BP) and the risk of cardiovascular events.<sup>2</sup> Inadequate control of BP is a leading risk factor for cardiovascular mortality worldwide as it contributes to 62% of the cerebrovascular accidents, 49% of the cases of ischemic heart disease and about 7.1 million deaths annually.<sup>3</sup> In the U.S. the incidence of AH continues to increase with age, but

recent data suggests improvement in terms of treatment and control.<sup>4</sup> In Europe lower frequencies of optimal drug control of AH are reported compared with those in the U.S.<sup>1</sup>

Several extensive studies, including INVEST, ACCOMPLISH, CONVINCENCE, ALLHAT, LIFE have registered failure in achieving the BP target levels with the therapeutic regimens set out in the study protocols. In these studies, 20 to 35% of participants did not reach the BP target levels despite receiving three antihypertensive drugs. In Bulgaria, the high incidence of cardiovascular morbidity and mortality

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## REVIEWS

### IS EVERYTHING CLEAR ABOUT TAKO-TSUBO SYNDROME?

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#### ABSTRACT

**INTRODUCTION:** Tako-tsubo syndrome is a novel cardio-vascular disease affecting predominantly postmenopausal women exposed to unexpected strong emotional or physical stress, in the absence of significant coronary heart disease. It is characterized by acute onset of severe chest pain and/or acute left ventricular failure, ECG-changes, typical left ventricular angiographic findings, good prognosis and positive resolution of the morphological and clinical manifestations. First described in 1990 in Japan by Sato, Tako-tsubo cardiomyopathy is characterized by transient contractile abnormalities of the left ventricle, causing typical left ventricular apical ballooning at end-systole with concomitant compensatory basal hyperkinesia. There are also atypical forms, presenting with left ventricular systolic dysfunction which affects the mid-portions of the left ventricle.

The etiology of the disease still remains unclear. Many theories have been put forward about the potential underlying pathophysiological mechanisms that may trigger this syndrome among which are the theory of catecholamine excess, the theory of multivessel coronary vasospasm, the ischemic theory, and the theory of microvascular dysfunction and dynamic left ventricular gradient induced by elevated circulating catecholamine levels.

Adequate management of Tako-tsubo syndrome demands immediate preparation for coronary angiography. Once the diagnosis is made, treatment is primarily symptomatic and includes monitoring for complications. Patients with Tako-tsubo syndrome most frequently develop acute LV failure, pulmonary edema, rhythm and conductive disturbances and apical thrombosis. Treatment is symptomatic and includes administration of diuretics, vasodilators and mechanical support of circulation with intra-aortic balloon counterpulsation.

**Key words:** *Tako-tsubo, apical ballooning, stress cardiomyopathy*

#### INTRODUCTION

The increasingly more frequent use of interventional techniques for diagnosing and management of acute coronary syndromes has brought about a more frequent differentiation of a specific syndrome of reversible stress-induced cardiomyopathy. Terms used to describe this condition in published reports include transient left ventricle apical ballooning syndrome, stress-induced cardiomyopathy, the broken-heart-syndrome, the ampullar syndrome, neurogenic stunned myocardium and Tako-tsubo cardiomyopathy.<sup>1,2</sup> The latter term has gained the widest currency in medical literature.

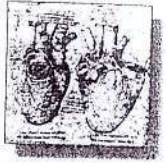
Tako-tsubo cardiomyopathy is a novel nosologic entity first described in 1990 by Sato<sup>3</sup> in Japan. It is characterized by transient contractile abnormality of the left ventricle which causes typical left

ventricular apical ballooning at end-systole with concomitant compensatory basal hyperkinesia.<sup>1</sup> This morphological finding resembles an octopus fishing pot used in Japan in the past which was called takotsubo (tako – octopus, tsubo – pot). This medical condition is characterized by transient left-ventricular (LV) systolic dysfunction with complete restoration of the contractile function to the normal within an interval of several days to a few weeks.<sup>2</sup>

Clinically, Tako-tsubo syndrome is characterized by a sudden onset of chest pain, manifestations of acute left ventricle failure with or without pulmonary edema, low cardiac output syndrome, wide spectrum of ECG changes such as ST-elevation, ST-depressions or deep T-wave inversions usually in the precordial leads, transient Q-waves, which

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## COVERED STENTS - TREATMENT OF CHOICE FOR SEVERE AORTIC COARCTATIONS AND ANEURYSMS IN ADOLESCENTS AND ADULTS?

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### Summary

*Objective:* To evaluate the early results of implantation of covered stents for aortic coarctations, recoarctations and thoracic aortic aneurysms.

*Background:* From an alternative to surgery stent implantation has become the treatment of choice for coarctation in adolescents and adults. However, aneurysm formation is reported after surgical repair, after balloon angioplasty, but also after stent implantation. Covered stents may overcome this problem but so far here is not enough data in the literature.

*Methods:* Fifteen consecutive patients (8 males, 7 females) have been scheduled for stent implantation between April 2003 and May 2006. The median age was 25.64 years (range 12-56). Eleven patients had native or residual Aortic coarctation (group I): Nine of them had native Aortic coarctations (four - with subatretic coarctation), two had recoarctations. Four patients had thoracic aortic aneurysms or pseudoaneurysms (group II): two of them after surgery for CoAo, one with Turner syndrome and one with a chronic dissecting aneurysm of the descending aorta.

*Results:* In group I five non-covered Cheatham-Platinum and six covered Cheatham-Platinum stents were implanted. The mean peak residual gradient was reduced from 45 (20-60) mmHg to 6 (0-20) mmHg, the mean coarctation diameter was increased from 6 (2.5-11) to 14.18 (12-24) mm. We had one major complication: a Cheatham-Platinum stent migrated to the abdominal aorta.

In group II four stent-grafts (two TAG endoprotheses, one Endofit endoprosthesis and one CCP-stent) were implanted in 3 patients. In all 3 cases complete exclusion of the aneurysm was achieved. One patient died of Ao-rupture before the procedure. There were no late complications. Multislice computed tomography showed no aneurysm formation with covered stents so far.

*Conclusion:* Implantation of covered stents gives very good early results in patients with severe Aortic coarctations and aneurysms and may become the treatment of choice for these entities.

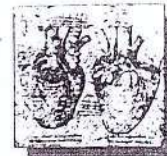
**Key words:** Aortic coarctation, Aortic aneurysm, covered CP stent, TAG endoprosthesis

### Abbreviations:

CoAo - coarctation of Aorta,  
CP - Cheatham-Platinum,  
CCP - covered Cheatham-Platinum,  
AoR - Aortic regurgitation.

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## EVALUATION OF NONHOMOGENIOUS LEFT VENTRICULAR REMODELING IN ARTERIAL HYPERTENSION BY REGIONAL LV WALL STRESS

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### Summary

Previous studies demonstrated the nonhomogeneity of concentric left ventricular (LV) remodeling in arterial hypertension (AH), which was associated with increased risk for these patients (pts).

Aim of the study: to investigate the LV remodeling in hypertension by the changes of regional LV wall stress.

Material and methods: Two groups were evaluated: (1) 21 pts (11 men and 10 women), mean age 49 (38-67) with AH and LV hypertrophy, without myocardial infarction (AH-group) and (2) 21 pts (13 men and 8 women), mean age 48 (34-56) with atypical chest pain, but normal ECG, echocardiography and coronarogram (control group). The regional LV wall stress was assessed by invasive modified Janz method for 5-segmental LV model.

Results: Statistical analysis showed higher end-diastolic regional stress (EDRS) in antero-lateral (AL) and apical (APIC) segments in AH-gr. vs. control gr. End-systolic regional stress (ESRS) was lower in AB and AL segments of LV with hypertrophy vs. controls. There was no differences in ESRS of APIC, ID and PB segments between the two groups. Linear positive correlations were found between elevated EDRS in AL, APIC segments and end-diastolic pressure in AH-gr. No correlation was found between LV wall thickness in AL segment and EDRS and ESRS changes in AH-gr., but ESRS in AB and AL segments correlated significantly to end-systolic pressure.

Conclusion: LV hypertrophy was a marker only for LV overload, whereas regional LV wall stress was the more complex parameter for evaluation the extent of nonhomogenous LV remodeling in AH.

**Key words:** regional LV wall stress, arterial hypertension, nonhomogenous, LV remodeling

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### Background

Assessment of left ventricular (LV) mass and LV wall thickness/chamber radius ratio (relative wall thickness) identified four different geometric patterns of LV adaptation to hypertension: concentric LV hypertrophy (increased mass and wall thickness), eccentric hypertrophy (increased mass, normal relative wall thickness), concentric remodeling (increased relative wall thickness with normal mass) and normal LV geometry.<sup>7</sup> Concentric hypertrophy was associated with especially high arterial pressure while eccentric hypertrophy - with elevated volume load and obesity.<sup>5</sup> Numerous studies showed that increased

LV mass could predict cardiovascular events and death independently of all conventional risk factors.<sup>1,4,12,14</sup> Adverse implications of low LV midwall function and high relative wall thickness were also identified.<sup>3,14</sup> The data strongly suggest that concentric LV remodeling, reflecting a nearly pure pressure overload was nonhomogenous and associated with poor prognosis.<sup>7,8,11</sup>

### Purpose

The aim of the study was to assess the nonhomogeneity of LV remodeling in hypertension by the changes of regional LV wall stress in end-diastole and end-systole.

# Role of Endovascular Recanalization and Stenting of Total Occlusions of The Renal Arteries For Blood Pressure Control in Resistant to Treatment Hypertension

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## Abstract

**Purpose:** To assess the effect on blood pressure (BP) control and rennin levels of the percutaneous recanalization of totally occluded renal arteries in patients with resistant arterial hypertension, preserved blood flow in the sub-segmental renal arteries, and high level of plasma rennin.

**Methods:** Between 2011 and 2015, we examined 7 patients with total occlusion of a Percutaneous recanalization was attempted in all of them. Success was achieved in 6 (85.7%) of the cases. All patients were hypertensive before the procedure, with mean BP values of 167.1/95.1 mmHg under systematic antihypertensive treatment with at least 3 antihypertensive agents. In all patients, plasma rennin activity levels were more than 2,5 ng/mL/h before the procedure. The patients had duplex signs of occluded renal artery and partially preserved subsegmental flow. Two of the patients showed normal serum creatinine levels, and one of them had CKD on chroniodialysis. The other three patients had slightly increased creatinine levels, and in two of them, creatinine levels normalized in the first follow-up month, and in the remaining patient, there was no significant change after the procedure. For recanalization of the occlusions of the renal arteries, we used coronary CTO techniques.

**Results:** Percutaneous recanalization of renal CTO was attempted in seven patients and was successful in six of the cases. Clinical and Duplex follow-up was performed at 4 weeks, 3 months, 6 months, and 1 year after the intervention. BP was significantly reduced in all of the patients who had undergone successful revascularization. Two cases of in stent restenosis showed increased BP levels, which normalized again after the second PTA. In all of the patients with successful procedure, normal rennin levels were established at 6 months and 1 year.

**Conclusion:** In cases of total renal artery occlusion, the most probable mechanism of resistant AH is the preserved microcirculation allowing juxtaglomerular cells survival resulting in elevated renin production. In case of renal occlusion and resistant AH, preserved renin production is a probable predictor of clinical success after recanalization. At the same time, preserved microcirculation perfusion is a predictor of renin-lowering effect and blood-pressure-control success after opening a renal CTO. There is evidence of a relationship between preserved parenchymal flow and the expected postinterventional result regarding BP control, confirmed in our cases. Endovascular recanalization of total renal artery occlusion is feasible and safe. This procedure has to be applied only to a selective group of patients with resistant hypertension and evidence of preserved subsegmental flow.

Abbreviations: BP: Blood Pressure ; RAS: Renal Artery Stenosis ; FMB: Fibro Muscular Dysplasia ; CTO: Chronic Total Occlusions ; ABPM: Ambulatory Blood Pressure Monitoring

## Introduction

Hypertension affects more than 25% of the worldwide adult population [1]. Although the vast majority of patients suffer from essential hypertension, it is important to identify patients with secondary treatable causes of hypertension, especially renal artery stenosis (RAS), which is the usual cause of hypertension

resistant to medical treatment [2]. The two main causes of renal artery stenosis are atherosclerosis and fibro muscular dysplasia (FMB). Atherosclerosis accounts for about 90% of all cases of RAS, while FMB is the cause of about 10%. FMD is most common in women between 20 and 50 years of age and its progression to total occlusion is rare, compared to that of atherosclerotic renal



# Cardiopoietic cell therapy for advanced ischemic heart failure: results at 39 weeks of the prospective, randomized, double blind, sham-controlled CHART-1 clinical trial

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<b>Aims</b>	Cardiopoietic cells, produced through cardiogenic conditioning of patients' mesenchymal stem cells, have shown preliminary efficacy. The Congestive Heart Failure Cardiopoietic Regenerative Therapy (CHART-1) trial aimed to validate cardiopoiesis-based biotherapy in a larger heart failure cohort.
<b>Methods and results</b>	This multinational, randomized, double-blind, sham-controlled study was conducted in 39 hospitals. Patients with symptomatic ischemic heart failure on guideline-directed therapy ( $n = 484$ ) were screened; $n = 348$ underwent bone marrow harvest and mesenchymal stem cell expansion. Those achieving $> 24$ million mesenchymal stem cells ( $n = 315$ ) were randomized to cardiopoietic cells delivered endomyocardially with a retention-enhanced catheter ( $n = 157$ ) or sham procedure ( $n = 158$ ). Procedures were performed as randomized in 271 patients ( $n = 120$ cardiopoietic cells, $n = 151$ sham). The primary efficacy endpoint was a Finkelstein–Schoenfeld hierarchical composite (all-cause mortality, worsening heart failure, Minnesota Living with Heart Failure Questionnaire score, 6-min walk distance, left ventricular end-systolic volume, and ejection fraction) at 39 weeks. The primary outcome was neutral (Mann–Whitney estimator 0.54, 95% confidence interval [CI] 0.47–0.61 [value $> 0.5$ favours cell treatment], $P = 0.27$ ). Exploratory analyses suggested a benefit of cell treatment on the primary composite in patients with baseline left ventricular end-diastolic volume 200–370 mL (60% of patients) (Mann–Whitney estimator 0.61, 95% CI 0.52–0.70, $P = 0.015$ ). No difference was observed in serious adverse events. One (0.9%) cardiopoietic cell patient and 9 (5.4%) sham patients experienced aborted or sudden cardiac death.
<b>Conclusion</b>	The primary endpoint was neutral, with safety demonstrated across the cohort. Further evaluation of cardiopoietic cell therapy in patients with elevated end-diastolic volume is warranted.
<b>Keywords</b>	Regenerative medicine • Cardiopoiesis • Cardiovascular disease • Stem cell • Target population • Disease severity • Marker • Precision medicine

## Introduction

Heart failure is a leading cause of mortality and morbidity; it limits quality of life and imposes a major societal burden.<sup>1</sup> Ischemic heart disease underpins two-thirds of all systolic heart failure.<sup>2</sup> Extensive myocardial remodelling and chamber enlargement portend poor outcomes, and standard treatments are often insufficient in such patients.<sup>3</sup> Cardiac transplantation or destination mechanical circulatory support remains high-risk therapeutic options that are further limited by donor availability, patient eligibility, and cost.<sup>4</sup>

By targeting myocardial restoration, cell-based therapies are alleged paradigm-shifting alternatives.<sup>5,6</sup> Clinical trials document reassuring feasibility and safety yet inconsistent efficacy, ascribed in part to unpredictable potency of cell products and limited retention.<sup>7,8</sup> These shortcomings impede advancement into cardiovascular practice.

Strategies for cell therapy optimization<sup>9</sup> include myocardial priming to improve cell homing,<sup>10</sup> exploiting resident cell populations<sup>11</sup> or leveraging combined cell regimens.<sup>12,13</sup> Guided cardiopoiesis is a recent option that enhances the cardioreparative functionality of patient-derived mesenchymal stem cells (MSC) and induces a restorative response in failing hearts.<sup>14</sup> The cardiopoietic phenotype demonstrated promise in proof-of-concept studies<sup>15</sup> and in the Cardiopoietic Stem Cell Therapy in Heart Failure (C-CURE) clinical trial.<sup>16</sup>

The Congestive Heart Failure Cardiopoietic Regenerative Therapy (CHART-1) trial was executed to validate the efficacy and safety of cardiopoietic cells delivered via an enhanced retention performance catheter<sup>17</sup> in a larger population with advanced symptomatic heart failure of ischemic aetiology.<sup>18</sup>

## Methods

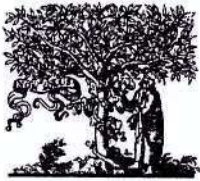
### Study design

The CHART-1 study is a prospective, multicentre, randomized, sham-controlled, patient- and evaluator-blinded clinical trial. Investigators at 39 centres in Europe and Israel participated (Figure 1 and Supplementary material online, Section 1). Ethics committee approvals were obtained for each participating centre. The CHART-1 trial was registered with clinicaltrials.gov (NCT01768702) and EudraCT (2011-001117-13). The study design has previously been described,<sup>18</sup> and the study protocol is provided in Supplement 2.

### Patients

Eligible patients gave written informed consent prior to any study-related procedures. Patients were not compensated for participation except for travel expenses. Patients were  $\geq 18$  to  $< 80$  years old with left ventricular ejection fraction (LVEF)  $\leq 35\%$  (locally interpreted echocardiograms were used for screening), ischemic heart failure without need for revascularization, heart failure hospitalization, or outpatient vasoactive heart failure therapy (e.g. vasodilators, positive inotropic agents, vasopressors or diuretics) within 12 months, in New York Heart Association (NYHA) class II or greater at screening, and with NYHA class III or IV or Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) class  $\geq 4$  within 12 months.<sup>18</sup> Guideline-directed medical therapy, a 6-min walk distance  $> 100$  to  $\leq 400$  m and Minnesota Living with Heart Failure Questionnaire (MLHFQ) score  $> 30$  were required. Acute coronary syndrome or percutaneous coronary intervention within 90 days, or coronary artery bypass graft surgery within 180 days were exclusions.<sup>18</sup> Eligible patients were scheduled for bone marrow harvest and MSC expansion.

Approximately 2 weeks after screening, bone marrow ( $\sim 65$ – $85$  mL) was collected from the iliac crest and shipped to a central production



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## Case report

## Successful endovascular treatment of type B aortic dissection in a 15-year-old child

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## ABSTRACT

Aortic dissection is a rare condition in the pediatric and young adult population [1]. Here, we present an unusual case of a 15-year-old male patient with sudden onset of chest and back pain and numbness in the left leg. Chest and abdominal CT revealed Stanford type B (DeBakey type III) aortic dissection, leading to subocclusive stenosis of the superior mesenteric artery (causing critical intestinal dysfunction with ileus) and total occlusion of left iliac and left renal arteries. The child was admitted 48 h after chest pain onset in critical clinical condition. Revascularization was achieved by several consecutive endovascular procedures, and the patient was discharged after favorable clinical evolution with full restoration of flow in the target organ arteries. The first interventional treatment included stenting of the superior mesenteric artery, stenting of the abdominal aorta, and balloon dilatation of the left iliac artery. Due to resistant renovascular hypertension, stenting of the left renal artery, which was occluded, was conducted 20 days later, leading to optimal blood pressure control. Thirty-three days following the initial procedure, an endovascular endograft prosthesis implantation was performed to close the primary tear in the thoracic aorta. Genetic samples revealed ACTA2 mutation. This case is extraordinary because of its combined life-threatening aortic and vessel pathology, treated for the first time with endovascular means in a child, and highlights the feasibility of endovascular treatment in the pediatric population. We discuss the imaging, management, and successful outcome of this severe condition.

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Abbreviations: AD, aortic dissection; CT, computed tomography; EVS, endovascular stenting; LSA, left subclavian artery; MRI, magnetic resonance imaging; PDA, patent ductus arteriosus.

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## Kasuistika | Case report

## A case of successful interventional treatment in acute basilar artery occlusion

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Supraselektivní trombolýza

## Keywords:

Acute basilar artery occlusion  
Cerebral angiography  
Mechanical thrombectomy  
Supraselective thrombolysis

## SOUHRN

Popisujeme případ úspěšné rekanalizace a příznivý klinický výsledek u pacienta s akutním uzávěrem bazilární tepny (basilar artery occlusion, BAO) a intervenční léčby (interventional treatment, IT). Sedmašedesátiletý muž byl přijat v komatózním stavu, s kvadraplegií a decerebrační rigiditou. Při příjmu byly zjištěny hodnoty skóre na stupnici GLCS (Glasgow-Liege Coma Scale), 24 na stupnici National Institutes of Health Stroke Scale (NIHSS) a 5 na modifikované Rankinově škále (modified Rankin Scale, mRS). Před IT byl pořízen nektrastní CT sken. Pro podezření na BAO bylo okamžitě provedeno angiografické vyšetření mozku, které prokázalo BAO mediálního a distálního segmentu. Léčba se prováděla intraarteriální katetrizací včetně balonkové angioplastiky a trombolýzy s aplikací 20 mg přípravku Actilyse (do 4 hodin od nástupu symptomů). Následné angiografické vyšetření potvrdilo optimální výsledek výkonu, po němž bylo na JIP pacientovi infuzně podáno během dalších tří hodin 10 mg přípravku Actilyse. Vzhledem ke zlepšení neurologického stavu byla o 12 hodin později provedena extubace. První den došlo k obnově vědomí a dokázal mluvit; další neurologický deficit nebyl zjištěn. Kontrolní CT neprokázalo nové známky ischemické cévní mozkové příhody. CT angiografie prokázala úplnou rekanalizaci distálního segmentu bazilární tepny a středně významnou reziduální stenózu v mediálním segmentu. Sedmý den po výkonu byl pacient propuštěn z nemocnice s hodnotami skóre NIHSS 7, GLCS 20 a mRS 3. Podle našeho názoru byla v našem případě léčba úspěšná díky rychle stanovené klinické diagnóze, rychlé dostupnosti katetizačního sálu a časně provedené mechanicko-farmakologické rekanalizaci.

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## ABSTRACT

We describe a case of successful recanalisation and favorable clinical outcome of a patient with acute basilar artery occlusion (BAO) and interventional treatment (IT). A 67-year old patient presented in a comatose state with quadriplegia, and decerebrate posturing. His initial Glasgow-Liege Coma Scale (GLCS) score was 11, National Institutes of Health Stroke Scale (NIHSS) 24, and modified Rankin Scale (mRS) 5. Non-contrast CT was performed before IT. Due to suspicion of BAO, an immediate cerebral angiography was performed. It demonstrated BAO in the middle and distal segment. Intra-arterial catheter based treatment was performed including balloon angioplasty and thrombolysis with 20 mg Actilyse (within four hours of symptoms onset). An optimal angiographic result was achieved. After the procedure the patient was treated in ICU with another 10 mg Actilyse infused over the next 3 hours. Because of neurological condition improving, the patient was extubated 12 hours later. On the first day, he regained consciousness, being able to speak, without new neurologic deficit. Control CT did not demonstrate new signs of ischemic stroke. CT angiography showed complete basilar artery recanalization in the distal part and a moderate residual stenosis in the middle segment. On the 7th day patient was discharged with NIHSS 7, GLCS 20, mRS 3. We believe that the success in our case was a result of the prompt clinical diagnosis, fast access to the cathlab and early mechanical-pharmacological recanalization.

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## Jacobs Journal of Clinical Case Reports

Case Report

### Complex Dysexecutive Syndrome and Agonistic Dyspraxia in a Patient with Bullous Pemphigoid

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#### Abstract

We are presenting a difficult diagnostic clinical case of a patient who developed a complex dysexecutive and disconnection syndrome with a rare form of hand apraxia, and bullous pemphigoid (BP). The differential diagnosis included a subacute toxic leukoencephalopathy and autoimmune encephalitis. The patient had a moderate exposure to propane-butane/CO, caused by a gas leak from a faulty household appliance. Reversible diffuse leukoencephalopathy with delayed evolution and toxic-hypoxemic etiology was our final diagnosis. It was made after a detailed study of our patient's medical history, and the extensive examinations conducted simultaneously. The possibility of autoimmune antibody-mediated non-vasculitic encephalitis, during severe BP, was excluded with serum, CSF, and antinuclear antibodies examination. The treatment assigned was non-specific, leading the patient to a very good recovery after a six-month period. Some of the key elements that helped us to identify the correct diagnosis and subsequently the appropriate therapy were: 1) Time-led graphic model of all the changes occurring throughout the development of his condition, providing us with a specific visual time-frame; 2) Analysis of the nonspecific brain MRI white matter changes; 3) The unique pattern of hand dyspraxia. This is a case of a rare primary neurological pathology and secondary skin involvement with BP. It also illustrates a favorable recovery after a broad white matter injury with a corpus callosum disconnection which caused a neuropsychiatric disorder and agonistic dyspraxia (AD).

**Keywords:** Agonistic Dyspraxia; Bullous Pemphigoid; Toxic-Hypoxemic Leukoencephalopathy

#### Abbreviations:

BP: Bullous Pemphigoid;

WMLEP: White Matter Leukoencephalopathy;

AD: Agonistic Dyspraxia;

MMSE: Mini Mental State Examination;

NIHSS: National Institute of Health Stroke Scale;



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## Original research article

# Diagnostic value of color-coded duplex sonography in patients with ischemic stroke and congenital changes in the circle of Willis

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## ABSTRACT

The circle of Willis (CoW) forms the main circulatory system in the human brain. A large number of variations of the CoW is known, and also their association with ischemic stroke.

Three cases of young patients with combination of ischemic stroke and anomalies in the CoW are presented, and the value of the color-coded duplex sonography (CCDS) is compared to other imaging diagnostics such as magnetic resonance angiography (MRA) and digital subtraction angiography (DSA).

In these patients we found multiple risk factors such as stenosis or thrombosis of intracranial brain vessels, mechanical compression of vessels, a genetic mutation associated with an increased risk of thrombosis, and intake of oral contraceptives. For clinical evaluation several methods were used: detailed medical history, neurological status, laboratory examinations (complete blood count, biochemistry, lipid profile, HIV1/2, Syphilis RPR test), screening for markers associated with an increased risk of thrombosis, chest X-ray, spinal fluid study, CCDS, DSA, MRA. A full conformity in the data from CCDS and other imaging methods was found.

The authors discuss the pathogenetic role of congenital anomalies of CoW, incidence of ischemic stroke and the high diagnostic value of CCDS for finding such anomalies.

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## Introduction

The circle of Willis (CoW) is the anastomosed arterial ring in the brain, which integrates the internal carotid and

vertebral-basilar systems. Sir Thomas Willis described the anatomy of the basal intracranial vessels for the first time in 1664.

There is considerable variability in the anatomy of the CoW, often with asymmetry, and to such extent that configuration

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## Kasuistika | Case report

## Minimally invasive treatment of a life threatening ruptured thoracic aortic aneurysm

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## SOUHRN

Popisujeme případ život ohrožující ruptury aneurysmatu hrudní aorty úspěšně řešené minimálně invazivním výkonem. Do naší nemocnice byl přijat 34letý muž v kritickém stavu, s akutní bolestí na hrudi po dobu 18 hodin, hemotemezí a s rychle klesajícími hodnotami hemoglobinu přes masivní transfuzi krve, s těžkou hypotenzí, anurií a se střevní obstrukcí. Ve věku 13 let podstoupil pacient operaci pro koarktaci aorty. CT skeny s použitím kontrastní látky prokázaly rupturu aneurysmatu hrudní aorty s těžkým levým hemothoraxem. Na základě pacientova celkového stavu, věku a anatomických poměrů léze bylo rozhodnuto o endovaskulární léčbě onemocnění sestupné hrudní aorty pomocí stentgraftů (thoracic endovascular aneurysm repair, TEVAR). Do hrudní aorty byly implantovány dva stentgrafty Valiant překrývající lézi primárního entry LSA. Vzhledem k reziduálnímu plnění aneurysmatického vaku levou podklíčkovou tepnou byl implantován vaskulární okludér; výsledkem byla úplná izolace aneurysmatu od krevního proudu s následným velmi krátkým a úspěšným obdobím zotavení. Poté byl pacient indikován k provedení video-asistované thorakoskopie (VATS) s cílem odstranit reziduální krevní sraženinu v levém pleurálním prostoru. Ruptura aortálního aneurysmatu je sice potenciálně fatální příhoda, pokud je však diagnostikována včas, lze ji úspěšně řešit endovaskulárně. V popsáném případě znamenalo naprosto nechirurgicky miniinvazivní řešení (TEVAR a uzávěr tepny ve snaze izolovat disekci a odstranění krevní sraženiny metodou VATS) účinný a život zachraňující výkon s rychlým zotavením bez dalších následků přes původně kritický stav při hospitalizaci.

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## ABSTRACT

We report a case of a life threatening thoracic aortic aneurysm rupture, treated successfully with minimally invasive approach. A 34-year-old man was admitted to our hospital in critical clinical condition, presenting with acute chest pain for 18 h, hematemesis and rapidly decreasing hemoglobin, despite massive transfusion done, severe hypotension, anuria and ileus. The patient had history of surgical aortic coarctation repair at age of 13. Contrast-enhanced CT images revealed a thoracic aortic aneurysm rupture with severe left-sided hemothorax. Based on the patient general condition, age and anatomy of the lesion thoracic endovascular aneurysm repair (TEVAR) was done. Two stent grafts Valiant were implanted in the thoracic aorta covering the entry tear engaging the LSA ostium. Because of residual filling of the aneurysmal sac through left subclavian artery, vascular occluder was implanted, causing complete isolation of the aneurysm from the blood flow. Very short and successful recovery period was observed. Due to residual coagulum in left pleural space the patient was directed for VATS evacuation. Aortic aneurysm rupture is a potentially fatal condition, but when diagnosed early, it can be successfully treated by endovascular methods. In this case a totally non-surgical minimally invasive approach (TEVAR and vascular plug to isolate the dissection and VATS assisted hemothorax evacuation) resulted efficiently and in a lifesaving manner with fast recovery without any sequelae despite the critical clinical presentation.

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## Original Investigation

# Effect of Darapladib on Major Coronary Events After an Acute Coronary Syndrome

## The SOLID-TIMI 52 Randomized Clinical Trial

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Supplemental content at  
jama.com

**IMPORTANCE** Lipoprotein-associated phospholipase A<sub>2</sub> (Lp-PLA<sub>2</sub>) has been hypothesized to be involved in atherogenesis through pathways related to inflammation. Darapladib is an oral, selective inhibitor of the Lp-PLA<sub>2</sub> enzyme.

**OBJECTIVE** To evaluate the efficacy and safety of darapladib in patients after an acute coronary syndrome (ACS) event.

**DESIGN, SETTING, AND PARTICIPANTS** SOLID-TIMI 52 was a multinational, double-blind, placebo-controlled trial that randomized 13 026 participants within 30 days of hospitalization with an ACS (non-ST-elevation or ST-elevation myocardial infarction [MI]) at 868 sites in 36 countries.

**INTERVENTIONS** Patients were randomized to either once-daily darapladib (160 mg) or placebo on a background of guideline-recommended therapy. Patients were followed up for a median of 2.5 years between December 7, 2009, and December 6, 2013.

**MAIN OUTCOMES AND MEASURES** The primary end point (major coronary events) was the composite of coronary heart disease (CHD) death, MI, or urgent coronary revascularization for myocardial ischemia. Kaplan-Meier event rates are reported at 3 years.

**RESULTS** During a median duration of 2.5 years, the primary end point occurred in 903 patients in the darapladib group and 910 in the placebo group (16.3% vs 15.6% at 3 years; hazard ratio [HR], 1.00 [95% CI, 0.91-1.09]; *P* = .93). The composite of cardiovascular death, MI, or stroke occurred in 824 in the darapladib group and 838 in the placebo group (15.0% vs 15.0% at 3 years; HR, 0.99 [95% CI, 0.90-1.09]; *P* = .78). There were no differences between the treatment groups for additional secondary end points, for individual components of the primary end point, or in all-cause mortality (371 events in the darapladib group and 395 in the placebo group [7.3% vs 7.1% at 3 years; HR, 0.94 [95% CI, 0.82-1.08]; *P* = .40). Patients were more likely to report an odor-related concern in the darapladib group vs the placebo group (11.5% vs 2.5%) and also more likely to report diarrhea (10.6% vs 5.6%).

**CONCLUSIONS AND RELEVANCE** In patients who experienced an ACS event, direct inhibition of Lp-PLA<sub>2</sub> with darapladib added to optimal medical therapy and initiated within 30 days of hospitalization did not reduce the risk of major coronary events.

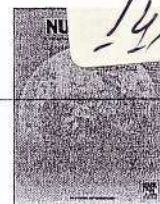
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## Special article

## Prevention strategies for cardiovascular diseases and diabetes mellitus in developing countries: World Conference of Clinical Nutrition 2013



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### Introduction

On Oct. 24 to 26, 2013, the 7th International Congress on Cardiovascular Diseases and the 17th World Congress on Clinical Nutrition took place in Sofia, Bulgaria ([www.iccsk.bizpa.in](http://www.iccsk.bizpa.in)). During the meetings, we reiterated that treatment decisions on cardiovascular disease (CVD) and diabetes mellitus should target the overall level of risks in each patient including biological risk

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# Reperfusion therapy for ST elevation acute myocardial infarction 2010/2011: current status in 37 ESC countries

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## Aims

Primary percutaneous coronary intervention (PPCI) is the preferred reperfusion therapy in ST-elevation myocardial infarction (STEMI). We conducted this study to evaluate the contemporary status on the use and type of reperfusion therapy in patients admitted with STEMI in the European Society of Cardiology (ESC) member countries.

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Original Investigation

# Anticoagulation With Otamixaban and Ischemic Events in Non-ST-Segment Elevation Acute Coronary Syndromes The TAO Randomized Clinical Trial

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**IMPORTANCE** The optimal anticoagulant for patients with non-ST-segment elevation acute coronary syndromes (NSTEMI-ACS) managed with an invasive strategy remains controversial.

**OBJECTIVE** To compare the clinical efficacy and safety of otamixaban, a novel intravenous direct factor Xa inhibitor, with that of unfractionated heparin plus downstream eptifibatid in patients with NSTEMI-ACS undergoing a planned early invasive strategy.

**DESIGN, SETTING, AND PARTICIPANTS** Randomized, double-blind, active-controlled superiority trial that enrolled 13 229 patients with NSTEMI-ACS and a planned early invasive strategy, at 568 active sites in 55 countries and conducted between April 2010 and February 2013. A planned interim analysis was conducted for otamixaban dose selection.

**INTERVENTIONS** Eligible participants were randomized to otamixaban (bolus and infusion, at 1 of 2 doses) or unfractionated heparin plus, at the time of percutaneous coronary intervention, eptifibatid. The otamixaban dose selected at interim analysis was an intravenous bolus of 0.080 mg/kg followed by an infusion of 0.140 mg/kg per hour.

**MAIN OUTCOMES AND MEASURES** The primary efficacy outcome was the composite of all-cause death or new myocardial infarction through day 7.

**RESULTS** Rates of the primary efficacy outcome were 5.5% (279 of 5105 patients) randomized to receive otamixaban and 5.7% (310 of 5466 patients) randomized to receive unfractionated heparin plus eptifibatid (adjusted relative risk, 0.99 [95% CI, 0.85-1.16];  $P = .93$ ). There were no differences for the secondary end points, including procedural thrombotic complications. The primary safety outcome of Thrombosis in Myocardial Infarction major or minor bleeding through day 7 was increased by otamixaban (3.1% vs 1.5%; relative risk, 2.13 [95% CI, 1.63-2.78];  $P < .001$ ). Results were consistent across prespecified subgroups.

**CONCLUSIONS AND RELEVANCE** Otamixaban did not reduce the rate of ischemic events relative to unfractionated heparin plus eptifibatid but did increase bleeding. These findings do not support the use of otamixaban for patients with NSTEMI-ACS undergoing planned early percutaneous coronary intervention.

**TRIAL REGISTRATION** [clinicaltrials.gov](http://clinicaltrials.gov) Identifier: NCT01076764

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ORIGINAL ARTICLE

# Effect of Platelet Inhibition with Cangrelor during PCI on Ischemic Events

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ABSTRACT

BACKGROUND

The intensity of antiplatelet therapy during percutaneous coronary intervention (PCI) is an important determinant of PCI-related ischemic complications. Cangrelor is a potent intravenous adenosine diphosphate (ADP)–receptor antagonist that acts rapidly and has quickly reversible effects.

METHODS

In a double-blind, placebo-controlled trial, we randomly assigned 11,145 patients who were undergoing either urgent or elective PCI and were receiving guideline-recommended therapy to receive a bolus and infusion of cangrelor or to receive a loading dose of 600 mg or 300 mg of clopidogrel. The primary efficacy end point was a composite of death, myocardial infarction, ischemia-driven revascularization, or stent thrombosis at 48 hours after randomization; the key secondary end point was stent thrombosis at 48 hours. The primary safety end point was severe bleeding at 48 hours.

RESULTS

The rate of the primary efficacy end point was 4.7% in the cangrelor group and 5.9% in the clopidogrel group (adjusted odds ratio with cangrelor, 0.78; 95% confidence interval [CI], 0.66 to 0.93; P=0.005). The rate of the primary safety end point was 0.16% in the cangrelor group and 0.11% in the clopidogrel group (odds ratio, 1.50; 95% CI, 0.53 to 4.22; P=0.44). Stent thrombosis developed in 0.8% of the patients in the cangrelor group and in 1.4% in the clopidogrel group (odds ratio, 0.62; 95% CI, 0.43 to 0.90; P=0.01). The rates of adverse events related to the study treatment were low in both groups, though transient dyspnea occurred significantly more frequently with cangrelor than with clopidogrel (1.2% vs. 0.3%). The benefit from cangrelor with respect to the primary end point was consistent across multiple prespecified subgroups.

CONCLUSIONS

Cangrelor significantly reduced the rate of ischemic events, including stent thrombosis, during PCI, with no significant increase in severe bleeding. (Funded by the Medicines Company; CHAMPION PHOENIX ClinicalTrials.gov number, NCT01156571.)

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\*The investigators in the Cangrelor versus Standard Therapy to Achieve Optimal Management of Platelet Inhibition (CHAMPION) PHOENIX trial are listed in the Supplementary Appendix, available at [NEJM.org](http://NEJM.org).

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