

JMAP2022サマナーセミナー

2022.8.28 Online Presentation

「慢性疾患重症化予防と地域連携」

戦略講演 「SGLT2阻害剤を活用した重症化予防：循環器分野と腎臓分野」

地域ぐるみで取り組む心不全重症化**予防**戦略
SGLT2阻害薬も含めて

やわたメディカルセンター 勝木達夫
(日本心臓リハビリテーション学会評議員、北陸支部長)



地域ぐるみで取り組む心不全重症化予防戦略 SGLT2阻害薬も含めて 「変わる」心不全診療

変わった **対象**、ガイドライン、診療報酬



変わる 薬物戦略 **SGLT2阻害薬** の心不全予防

変わるべき 地域ぐるみの**心臓リハビリテーション**





 **やわたメディカルセンター**
YAWATA MEDICAL CENTER
病気にならないための病院

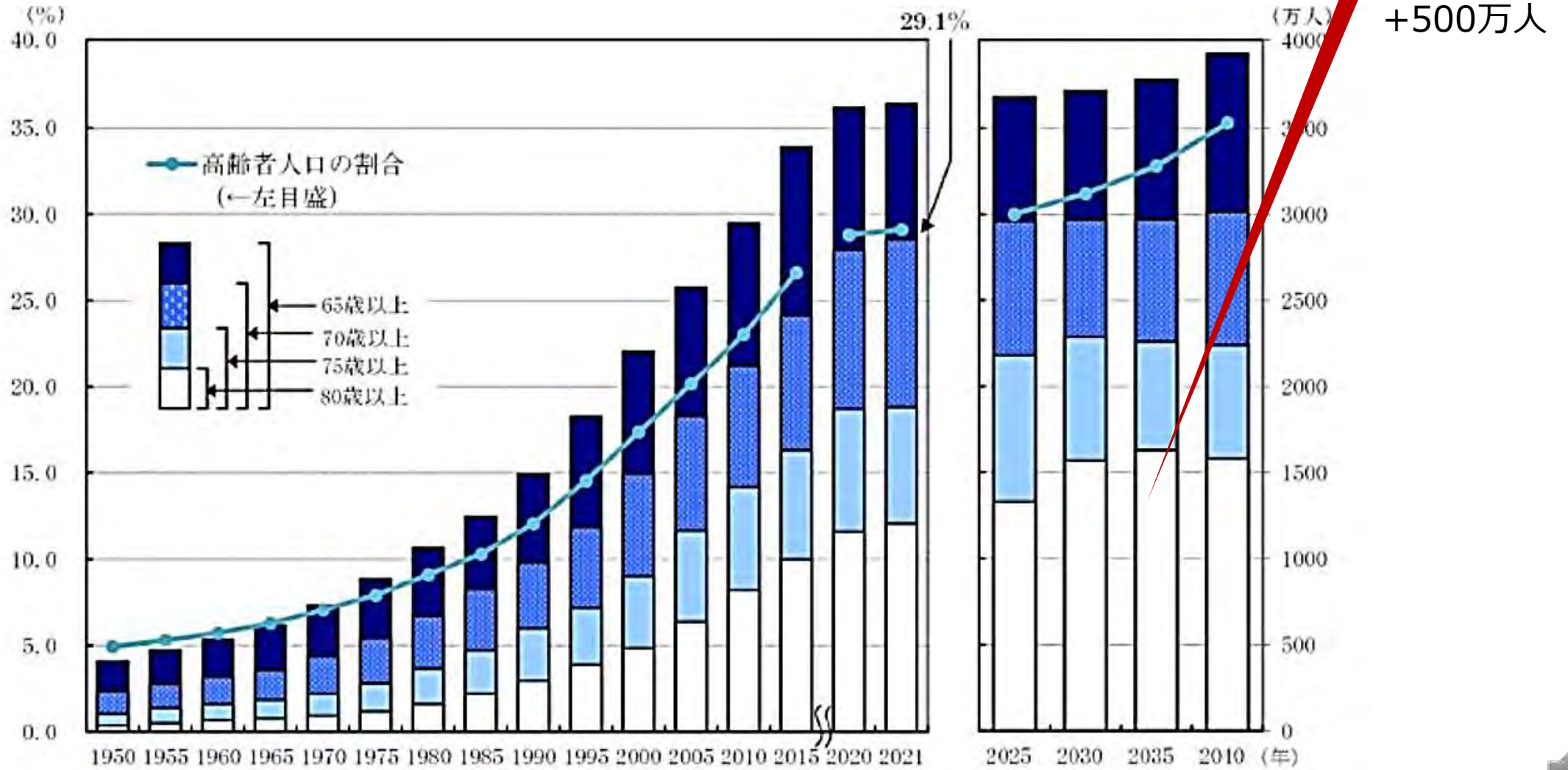


変わる対象



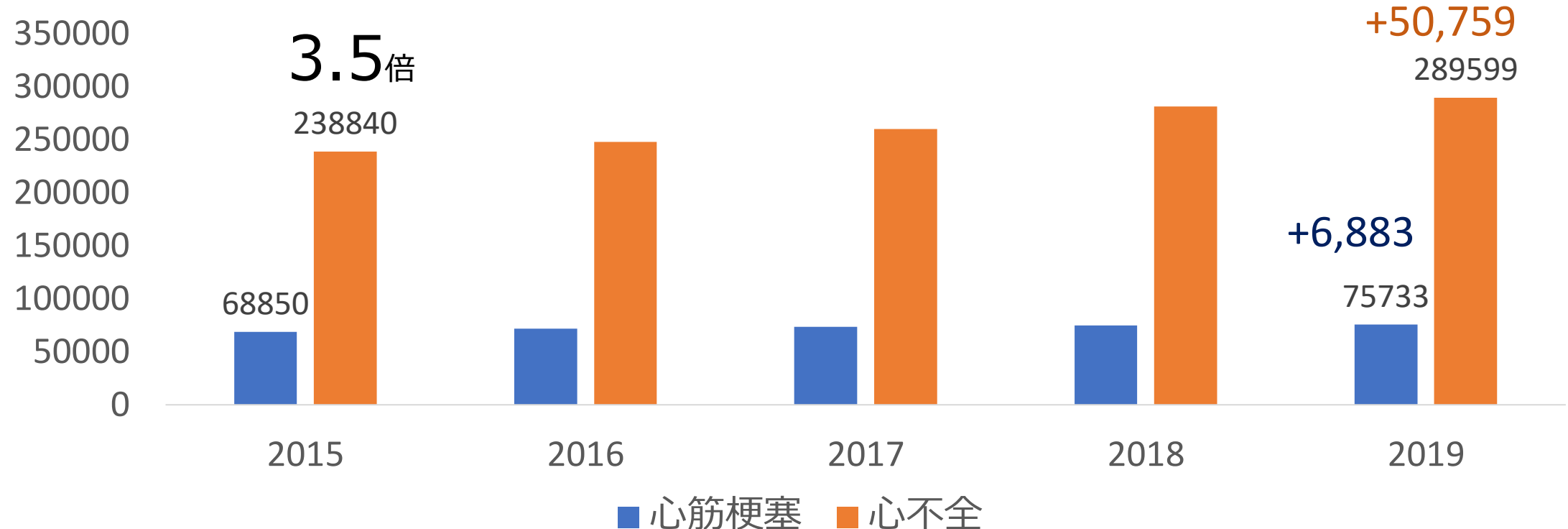
増える高齢者人口

80歳以上 2035年まで増える



心筋梗塞10%増、心不全21%増

患者数



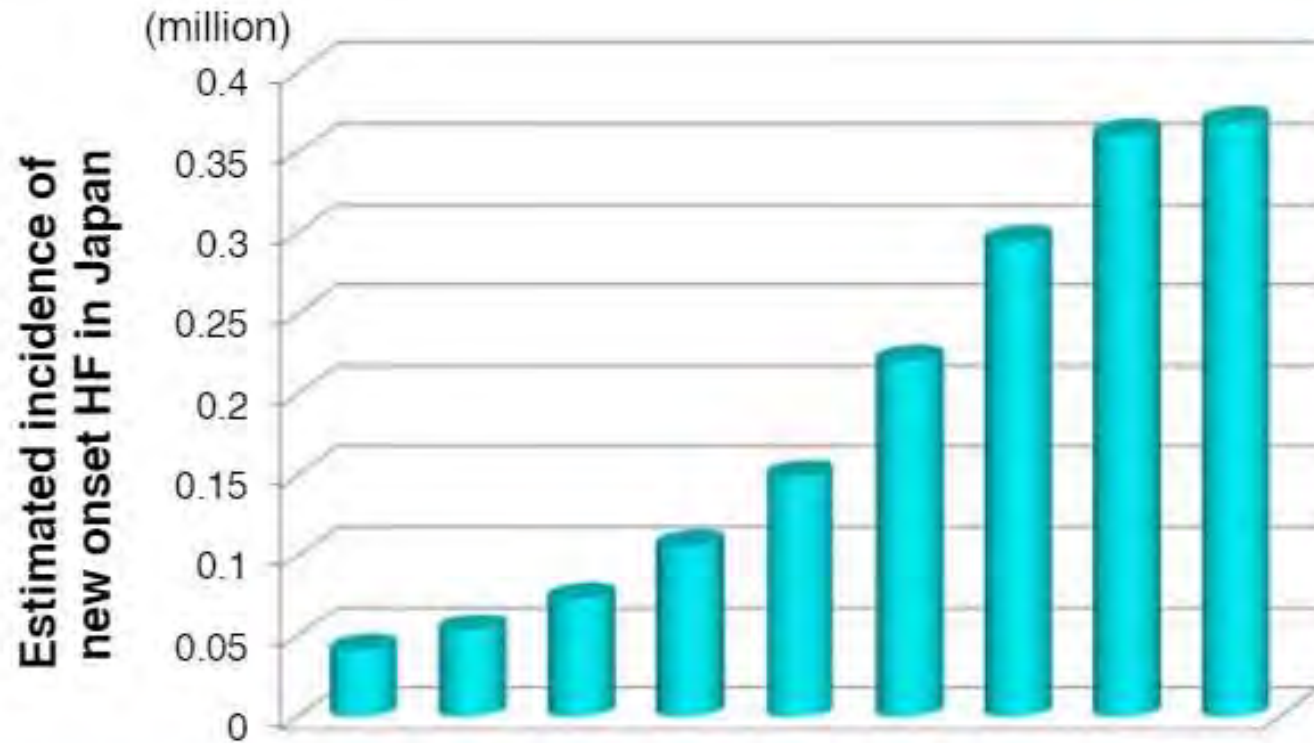
新規心不全発症はこれからも増える

Heart failure as a general pandemic in Asia

Hiroaki Shimokawa*, Masanobu Miura, Kotaro Nochioka, and Yasuhiko Sakata



European Journal of Heart Failure (2015) 17, 884–892
doi:10.1002/ejhf.319



Year	1950	1960	1970	1980	1990	2000	2010	2020	2030
% of the elderly (≥65 years)	4.9	5.7	7.1	9.1	12.1	17.4	23.0	29.1	31.6
Total population in Japan (million)	83.2	93.4	103.7	117.1	123.6	126.9	128.1	124.1	116.6



Characteristics of Elderly Patients with Heart Failure and Impact on Activities of Daily Living: A Registry Report from Super-Aged Society

HIROAKI OBATA, MD, PhD,^{1,3} TOHRU IZUMI, MD, PhD,^{1,3} MASASHI YAMASHITA, PhD,^{2,3} WATARU MITSUUMA, MD, PhD,¹
KEISUKE SUZUKI, MD, PhD,¹ SHINICHI NOTO, PhD,⁴ TAKESHI MORIMOTO, MD, PhD, MPH,⁵ AND
MITSUAKI ISOBE, MD, PhD^{3,7}

Niigata, Sanyamihara, Nishitomiya, and Japan

地方都市（新潟）での心不全入院 80歳以上で75%超

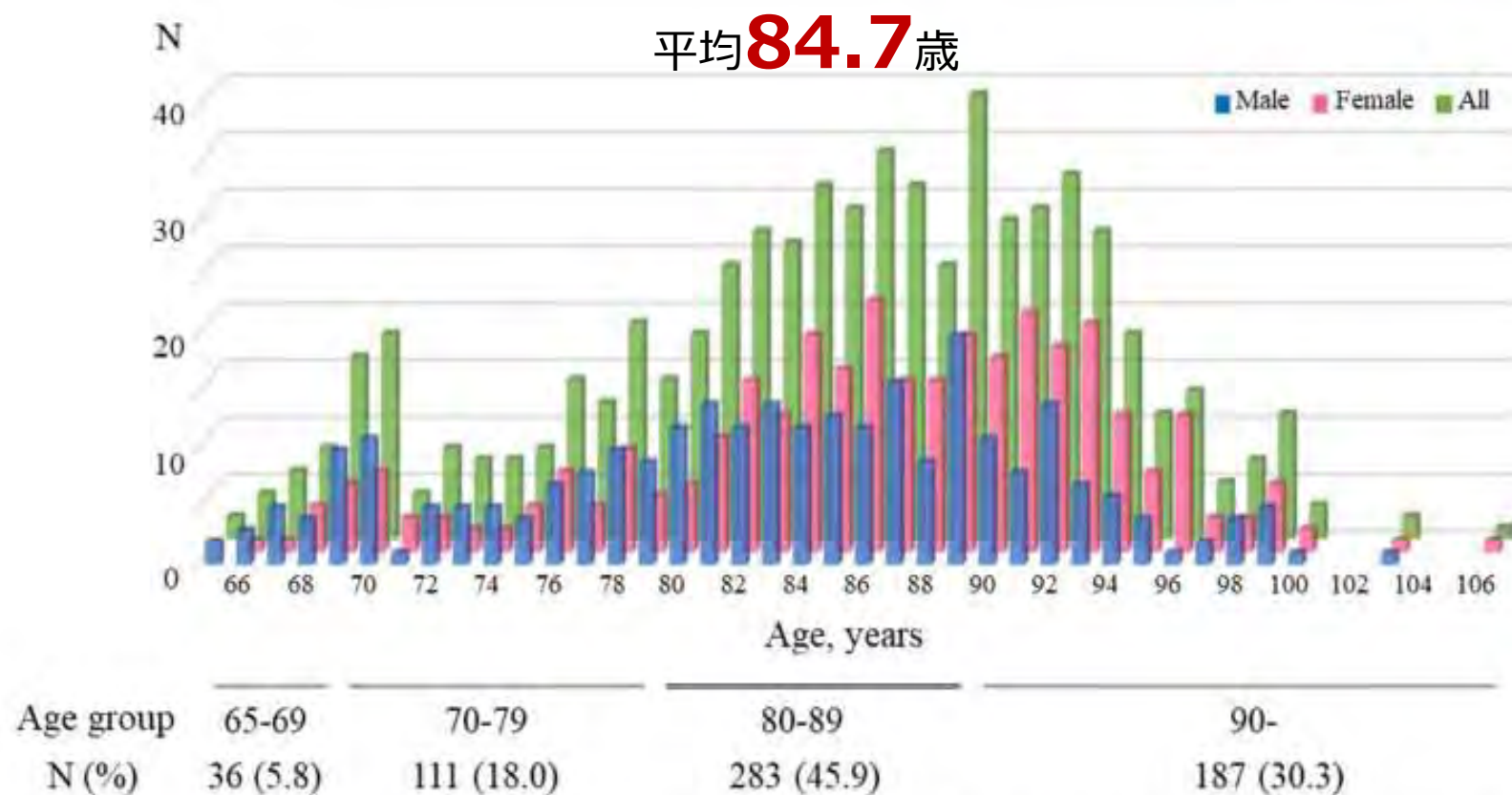


Fig. 1. Age distribution of the patients. The distribution of elderly patients with heart failure admitted to community-based hospitals peaked in the 80–89 age group for both men and women.



HFpEFは増加

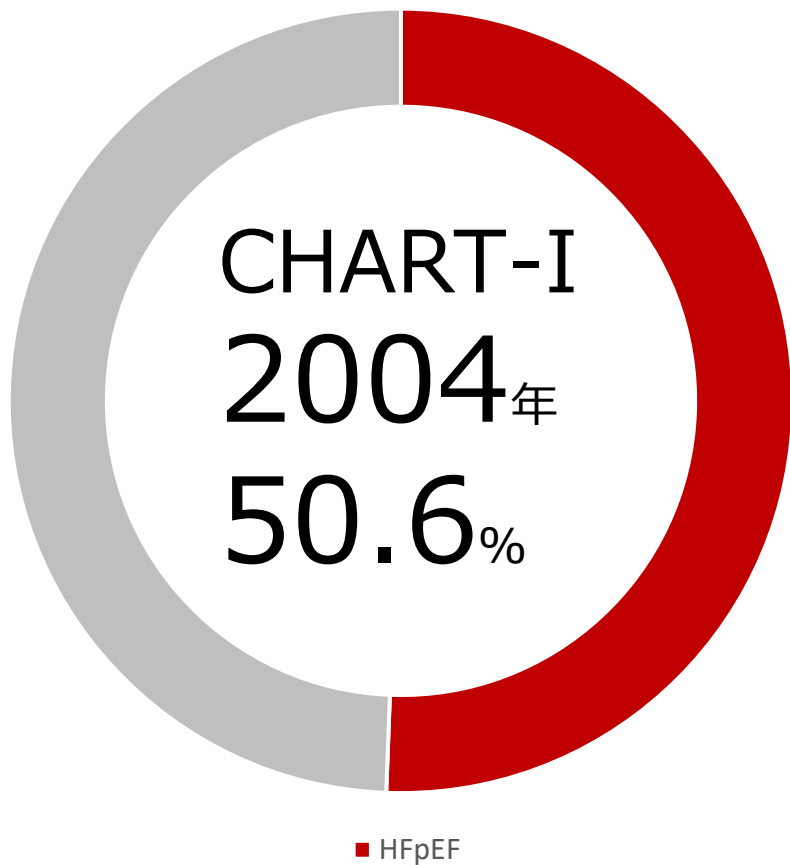


CHART-I Circ J 2004;68:427-434.

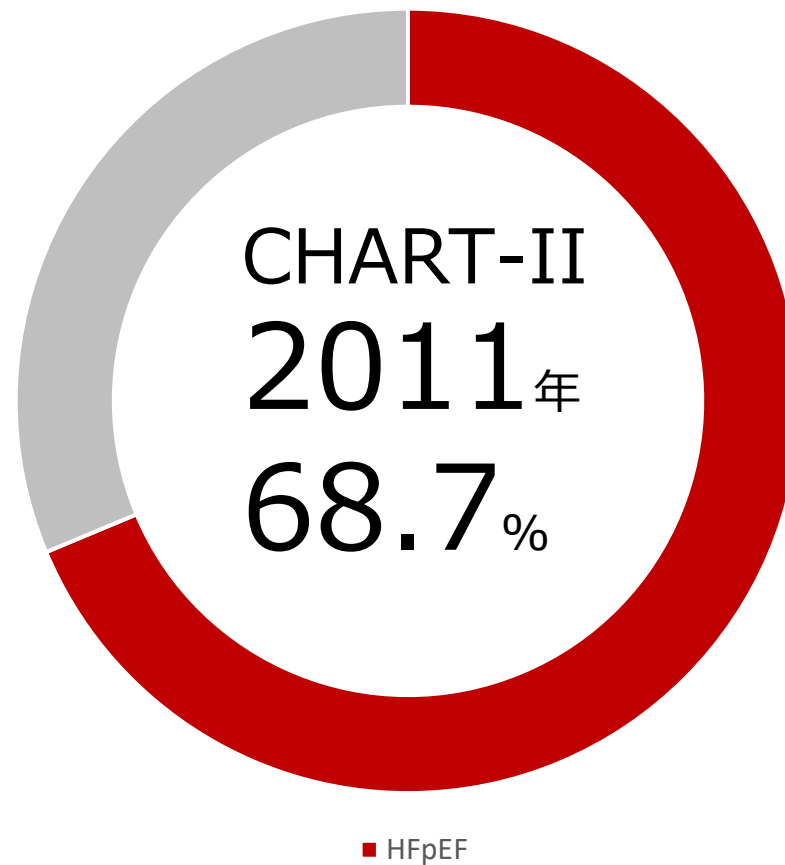


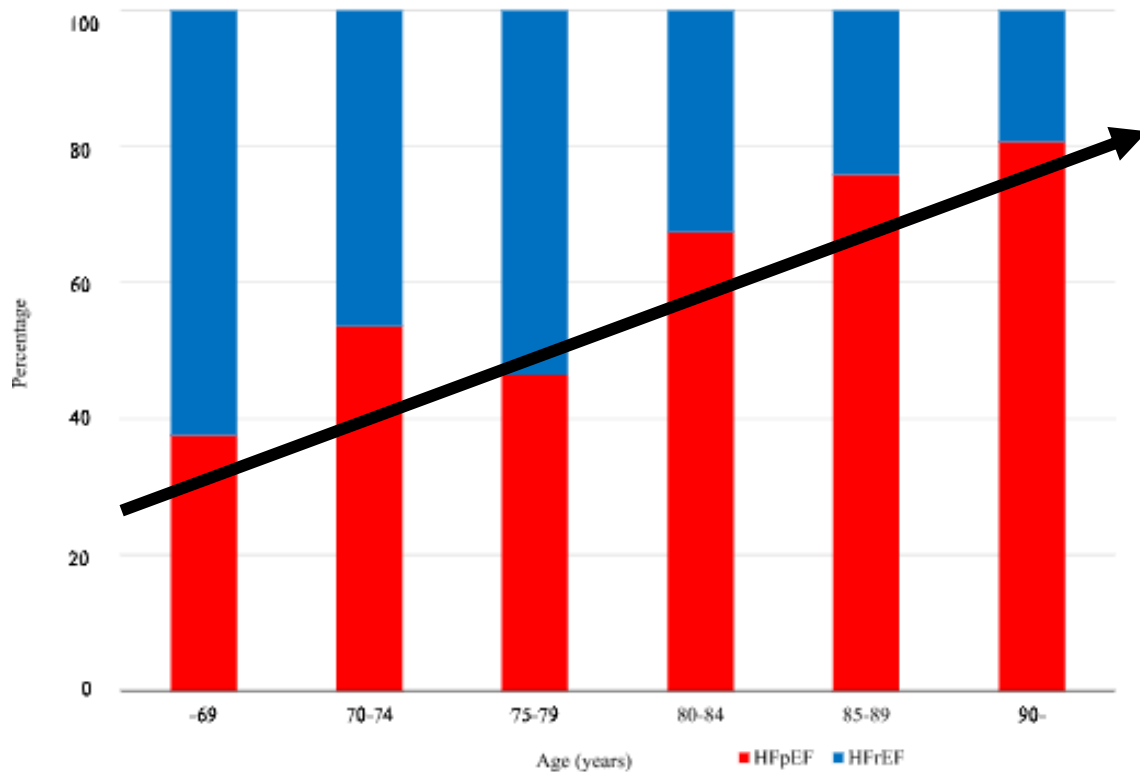
CHART-II Circ J 2011;75:823-833.

Clinical characteristics and frailty status in heart failure with preserved vs. reduced ejection fraction

Tomoyuki Hamada¹, Toru Kubo¹, Kazuya Kawai², Yoko Nakaoka², Toshikazu Yabe³, Takashi Furuno⁴, Eisuke Yamada⁵, Hiroaki Kitaoka^{1*} and Koichi YOSACOI study

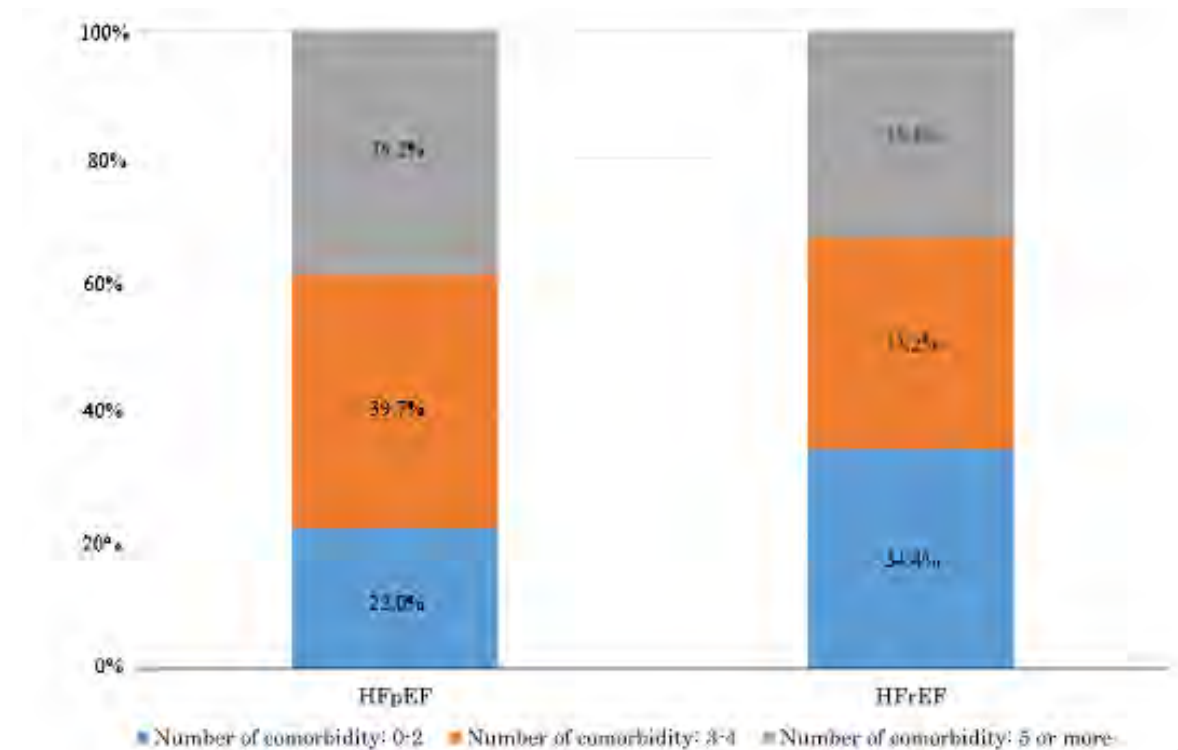
¹Department of Cardiology and Geriatrics, Kochi Medical School, Kochi University, Kochi, 783-8585, Japan; ²Department of Cardiology, Chikamori Hospital, Kochi, Japan; ³Department of Cardiology, Kochi Prefectural Hazakuraei Hospital, Sukumo, Japan; ⁴Department of Cardiology, Kochi Prefectural Aki General Hospital, Aki, Japan; and ⁵Department of Cardiology, Sasaki Rukusho Hospital, Sasaki, Japan

高齢になるほどHFpEF比率が高い



YOSAKOI study HFpEFの方が**フレイル**が多い

HFpEFでは重複障害 ≥ 3 が8割超



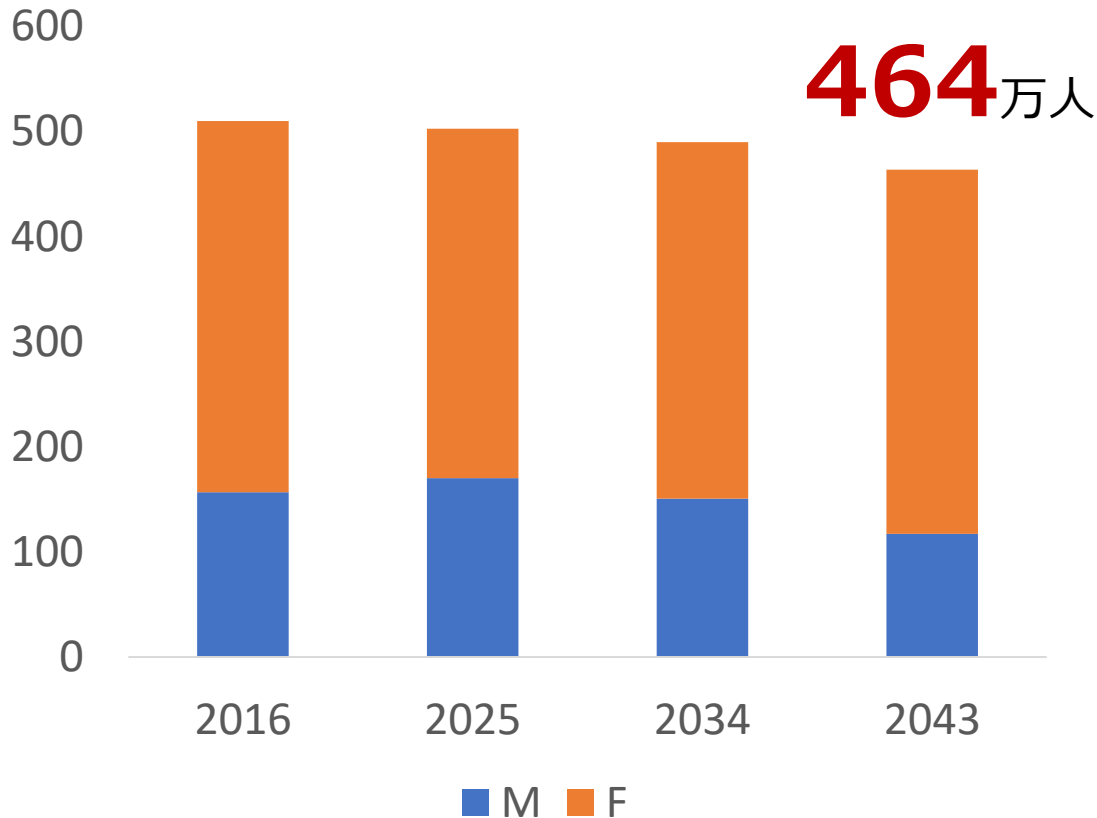
Projecting prevalence of frailty and dementia and the economic cost of care in Japan from 2016 to 2043: a microsimulation modelling study

Megumi Kasajima, Karen Eggleston, Shoki Kusaka, Hiroki Matsui, Tomoki Tanaka, Bo-Kyung Son, Katsuya Iijima, Kazuo Goda, Masaru Kitsuregawa, Jay Bhattacharya, Hideki Hashimoto

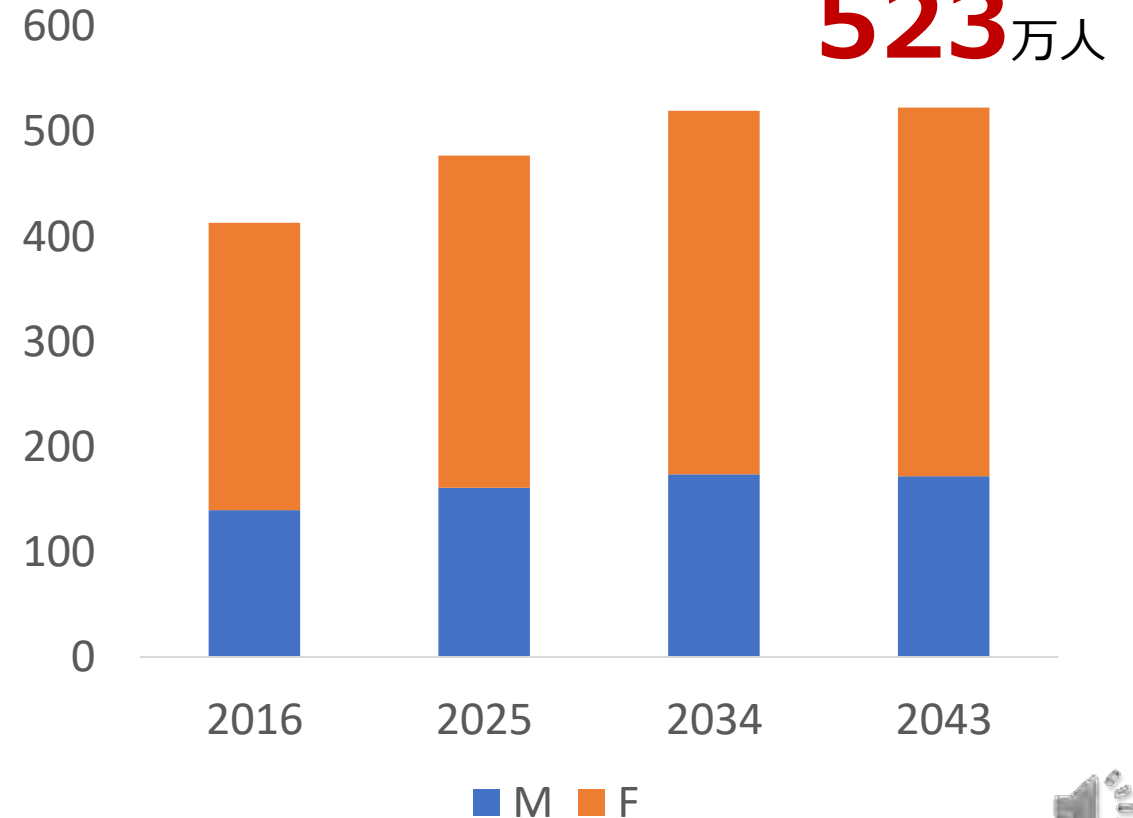


20年後の未来予想
認知症<フレイル
低学歴例有症率増
介護費用増、格差拡大

認知症



フレイル



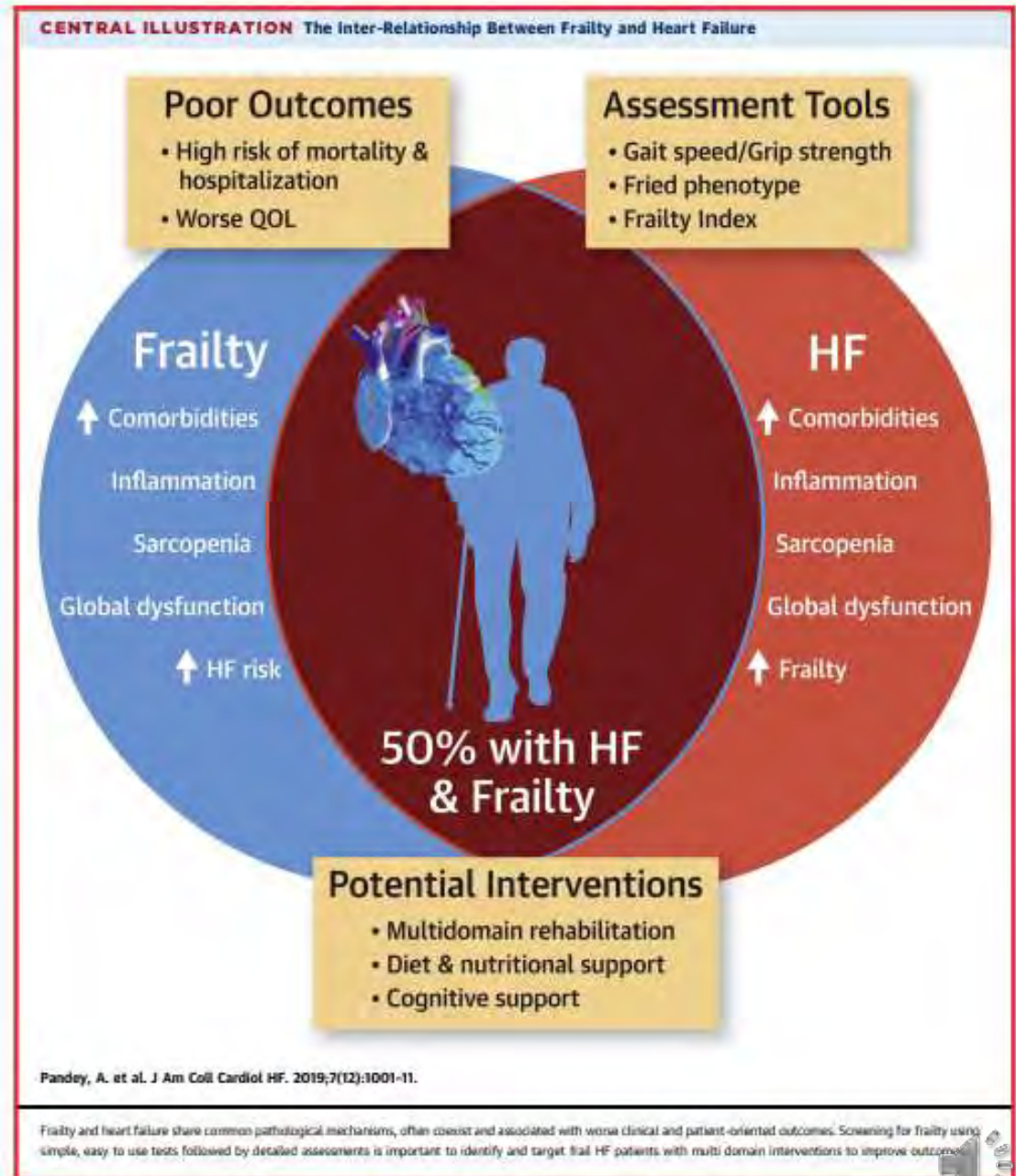
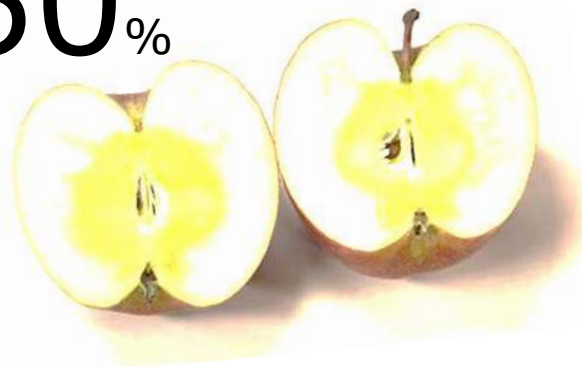
Frailty Is Intertwined With Heart Failure

Mechanisms, Prevalence, Prognosis, Assessment, and Management

Ambarish Pandey, MD, MSCS,^a Dalane Kitzman, MD,^b Gordon Reeves, MD, MPT^c

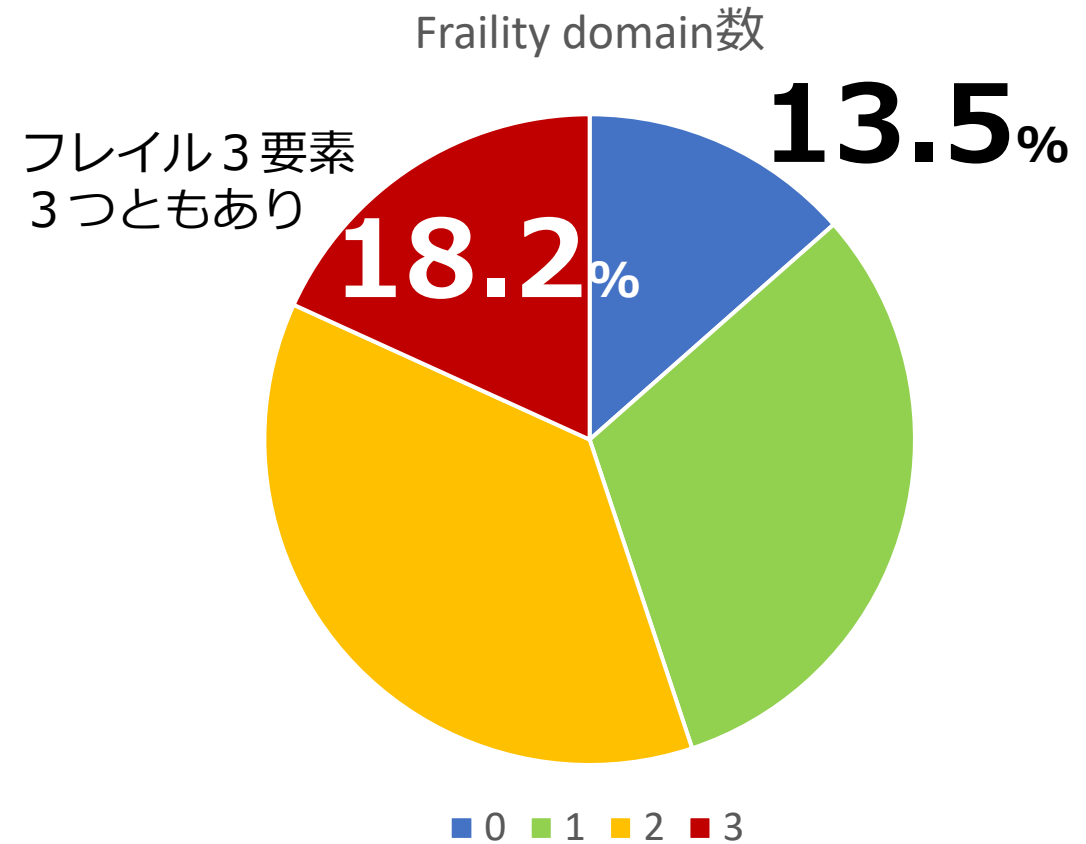
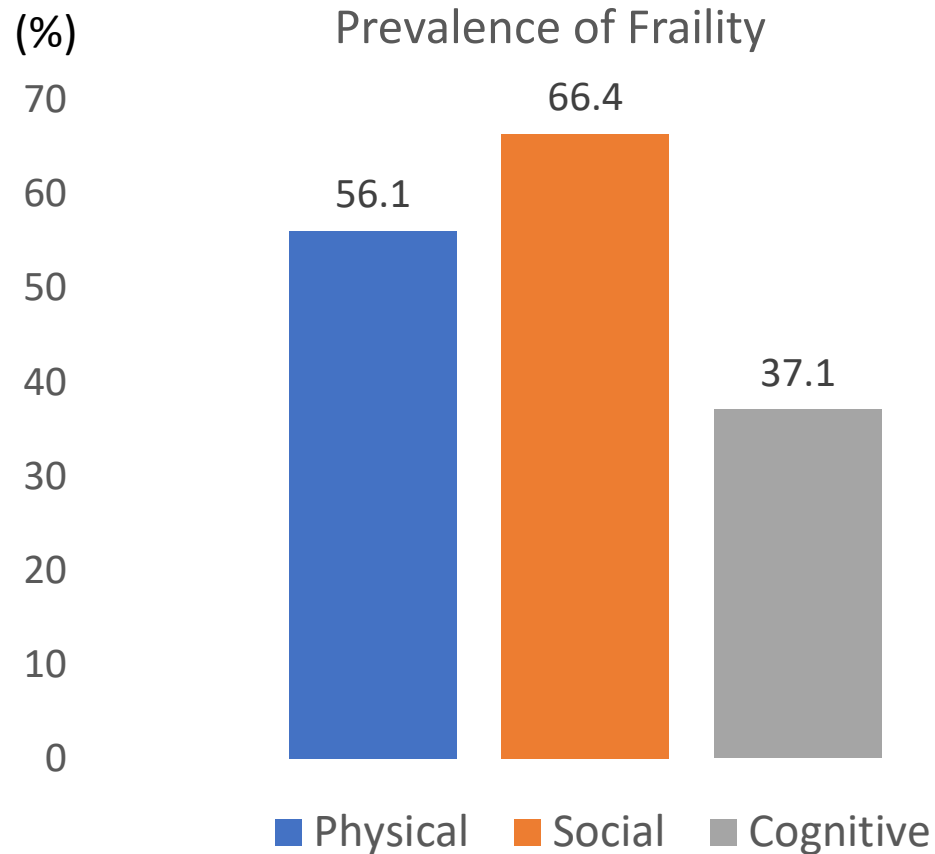
www.jacc.org/doi/pdf/10.1016/j.jchf.2019.10.005

50%



Prevalence and prognostic impact of the coexistence of multiple frailty domains in elderly patients with heart failure: the FRAGILE-HF cohort study

ESC HF 2020;22:2112-2119



Original article

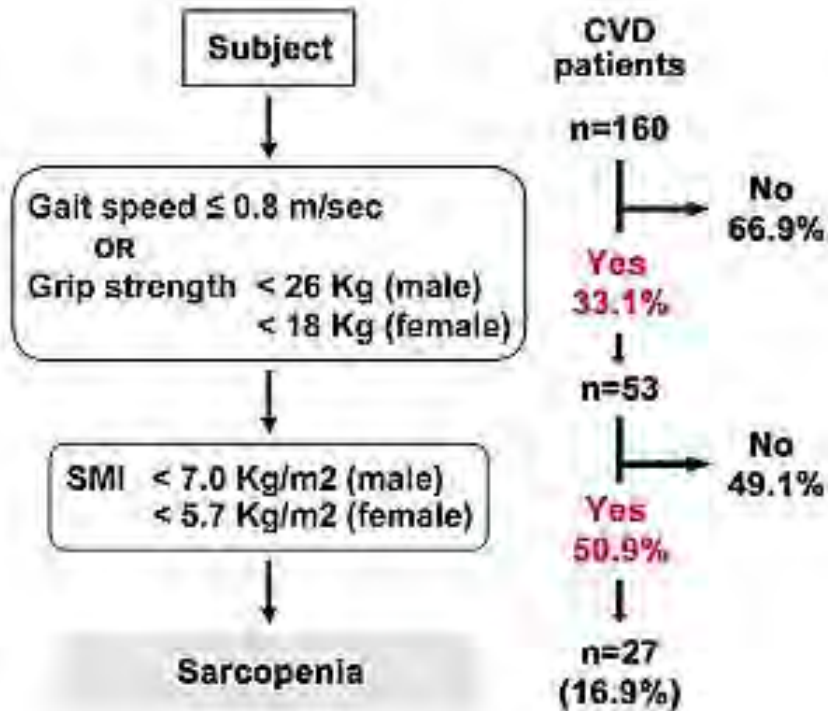
The prevalence of sarcopenia and subtypes in cardiovascular diseases, and a new diagnostic approach

Ken-ichiro Sasaki (MD, PhD)^{a,*}, Tatsuyuki Kakuma (PhD)^b, Motoki Sasaki (MD)^c, Yuta Ishizaki (MD)^d, Aiko Fukami (MD, PhD)^e, Mika Enomoto (MD, PhD)^f, Hisashi Adachi (MD, PhD)^g, Hiroo Matsuse (MD, PhD)^h, Naoto Shiba (MD, PhD)ⁱ, Takafumi Ueno (MD, PhD)^j, Yoshihiro Fukumoto (MD, PhD, FJCC)^k

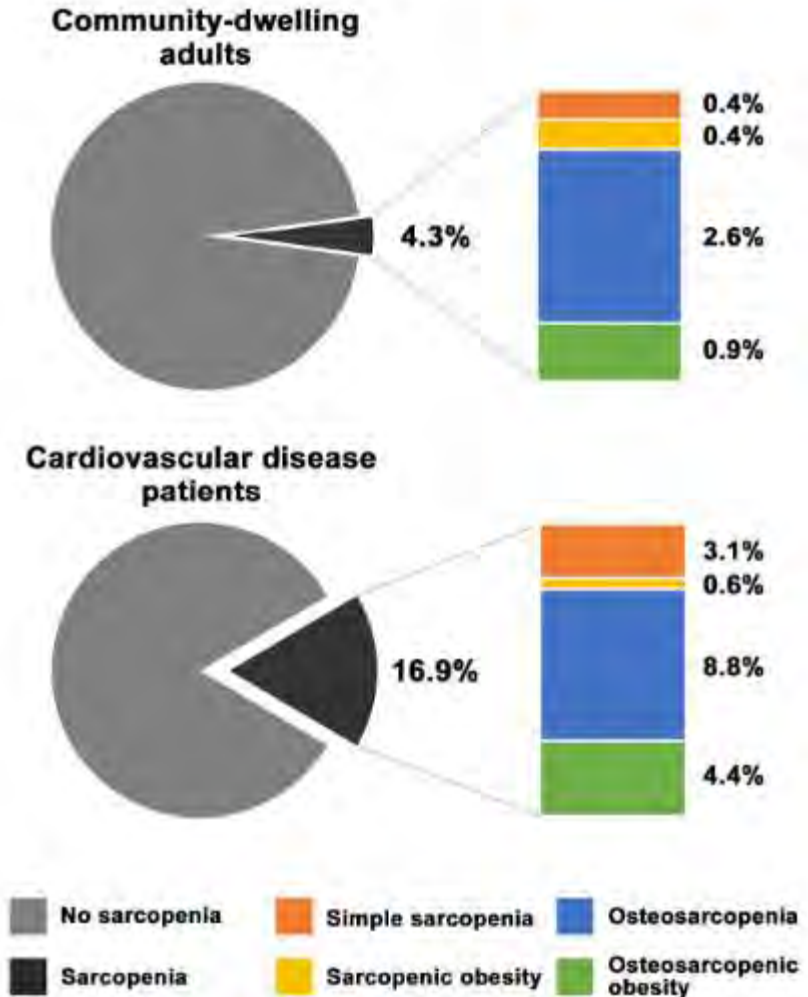
^aDivision of Cardiovascular Medicine, Department of Internal Medicine, Kurume University School of Medicine, Kurume, Japan

^bBiostatistics Center, Kurume University, Kurume, Japan

^cDepartment of Rehabilitation, Kurume University Hospital, Kurume, Japan



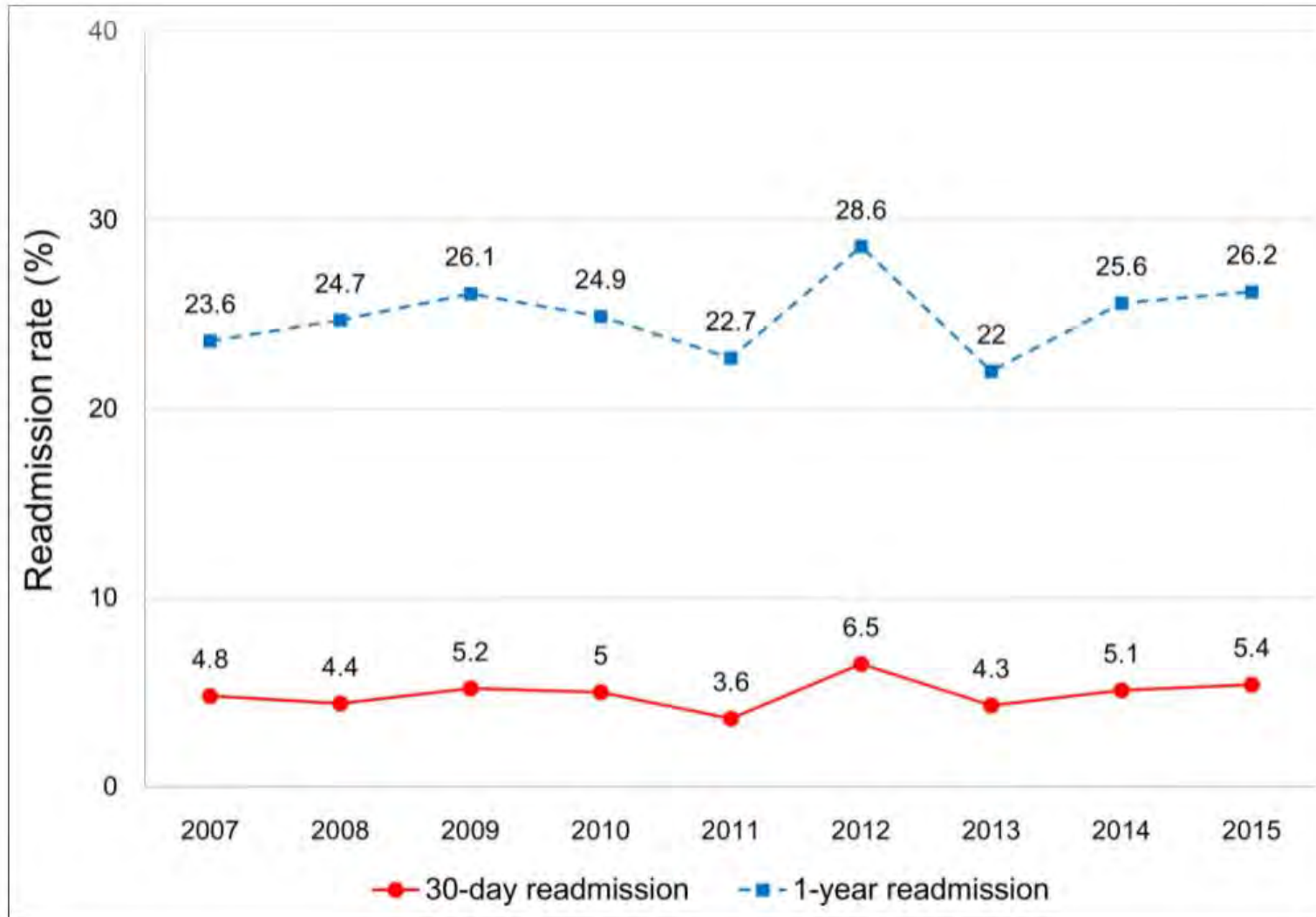
心疾患患者はサルコペニア 4 倍 心不全なら 6 倍



9-Year Trend in the Management of Acute Heart Failure in Japan: A Report From the National Consortium of Acute Heart Failure Registries

Yasuyuki Shiraishi, MD; Shun Kohsaka, MD; Naoki Sato, MD; Teruo Takano, MD; Takeshi Kitai, MD; Tsutomu Yoshikawa, MD; Yuya Matsue, MD

J Am Heart Assoc. 2018;7:e008687.
<https://doi.org/10.1161/JAHA.118.008687>



心不全**再**入院率は**変わらず**高率

1月 5% —
1年 25% - - -



100万円/回

Hospitalization Costs for Patients
With Acute Congestive Heart Failure in Japan

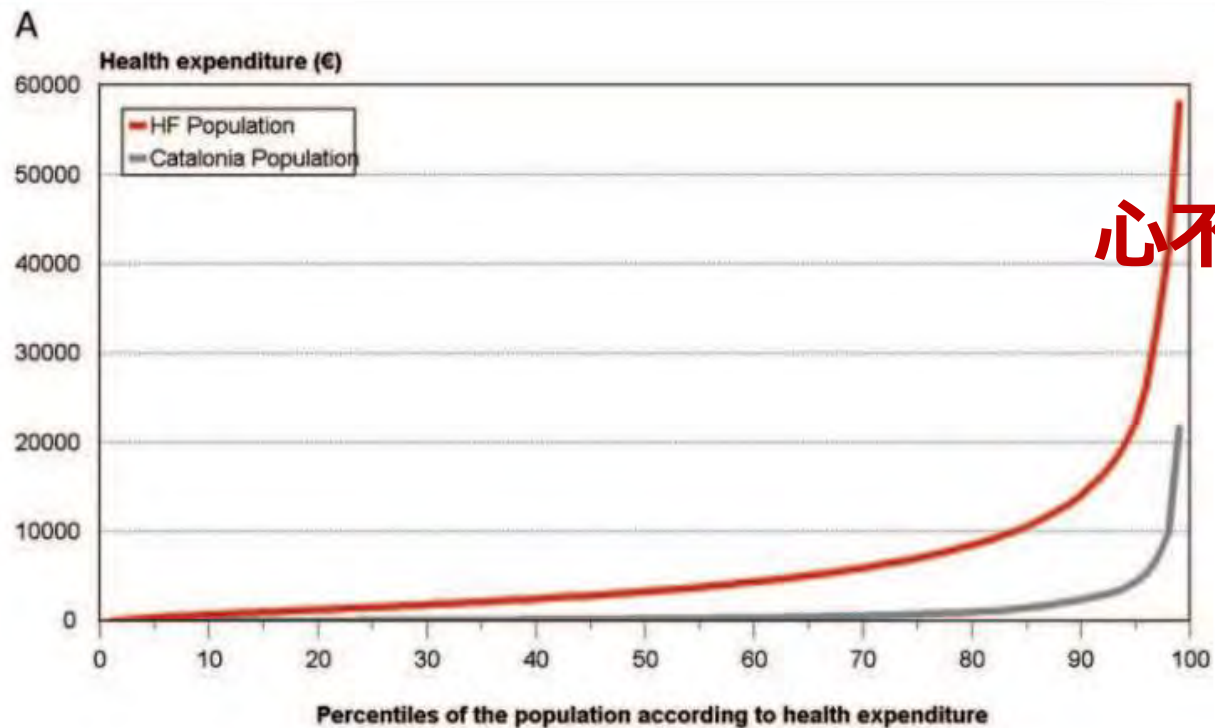
Median Costs **\$8,809** per episode

[Circ J.](#) 2019 Apr 25;83(5):1025-1031



Medical resource use and expenditure in patients with chronic heart failure: a population-based analysis of 88 195 patients

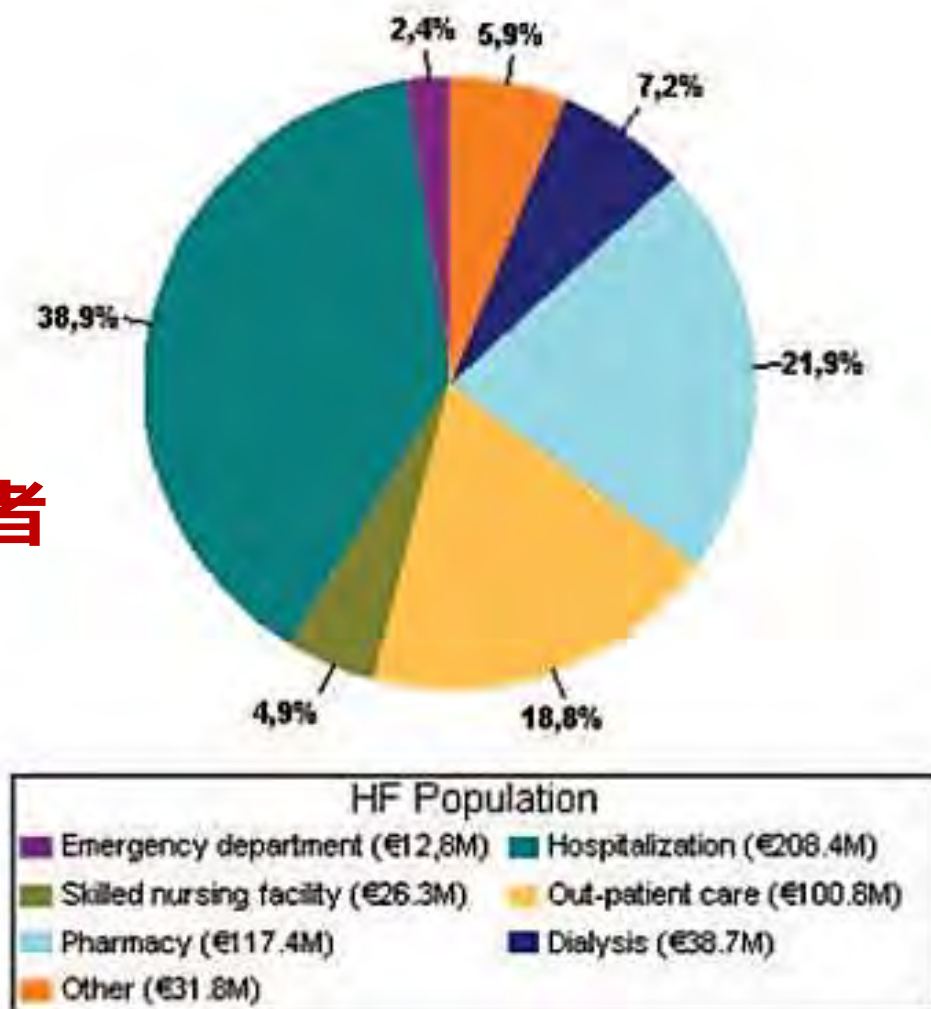
Nuria Farré^{1,2}, Emili Vela³, Montse Clèries³, Montse Bustins³, Miguel Cainzos-Achirica^{4,5}, Cristina Enjuanes^{1,2,6}, Pedro Moliner^{1,2,6}, Sonia Ruiz^{1,2}, Jose Maria Verdú-Rotellar^{2,6,7}, and Josep Comin-Colet^{1,2,6*}



心不全患者

一般

心不全患者医療費は高額
入院費 4 割



変わったガイドライン



2002年、2007年、2012年を踏まえて

2021年8月31日更新
2021年3月27日発行

日本循環器学会 / 日本心臓リハビリテーション学会合同ガイドライン

2021年改訂版

心血管疾患におけるリハビリテーションに関する ガイドライン

JCS/JACR 2021 Guideline on Rehabilitation in Patients with Cardiovascular Disease

合同研究班参加学会

日本循環器学会 日本心臓リハビリテーション学会
日本冠疾患学会 日本胸部外科学会 日本循環器看護学会
日本小児循環器学会 日本心臓病学会 日本心不全学会 日本病態栄養学会
日本不整脈心電学会 日本理学療法士協会 日本臨床スポーツ医学会



改訂のポイント

運動療法中心から疾病管理プログラムへ

第7章 栄養と食事療法

第8章 QOLおよび精神心理学的評価と介入

第9章 患者教育と疾病管理

第10章 運営に関する課題

新しいターゲット 第5章 特別な患者群におけるリハビリテーション

フレイル、サルコペニア（高齢心疾患患者）

経カテーテル大動脈弁置換術（TAVI）後

植込み型除細動器（ICD）などのデバイス植込み後

肺高血圧

大動脈ステントグラフト内挿術後

補助人工心臓装着後、心移植後

腫瘍循環器



改訂のポイント

運動耐容能からQOLへ

虚血性心疾患中心から高齢フレイル心不全中心へ

求められる新たな展開

遠隔医療

在宅医療

緩和ケア

地域包括ケアシステム



急性・慢性心不全診療ガイドライン (2017年改訂版)

Guidelines for Diagnosis and Treatment of Acute and Chronic Heart Failure
(JCS 2017/JHFS 2017)

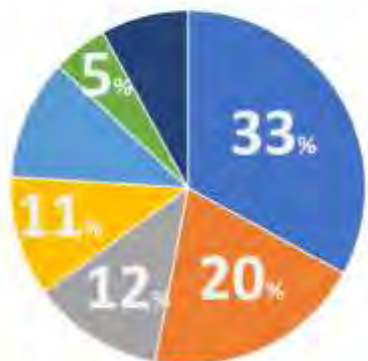
参画研究団体の学会・研究班

日本循環器学会 日本心不全学会 日本胸外科学会
日本高血圧学会 日本心エコー図学会 日本心臓血管外科学会
日本心臓病学会 日本心臓リハビリテーション学会 日本超音波医学会
日本糖尿病学会 日本不整脈心電学会
厚生労働省 難治性疾患政策研究事業「特発性心筋症に関する調査研究」研究班
日本医療研究開発機構 難治性疾患実用化研究事業「拡張相肥大型心筋症を対象とした多施設登録観察研究」研究班

V. 心不全治療の基本方針

心不全増悪による再入院の要因 セルフケアの重要性

Jpn Circ J 2000改変



- 塩分、水分
- 感染症
- 薬
- 過労
- 不整脈
- ストレス
- その他

2.

心不全治療のアルゴリズム (図10)

心不全の経過は多くの場合、慢性・進行性である。大多数の心不全は急性心不全として発症するが、代償化され慢性心不全(ステージC心不全ステージ)に移行する。その後は慢性に進行するが、急性増悪により非代償性急性心不全を反復しやすい。急性増悪を反復することにより徐々に重症化していく。さらに経過中に突然死をきたすことも

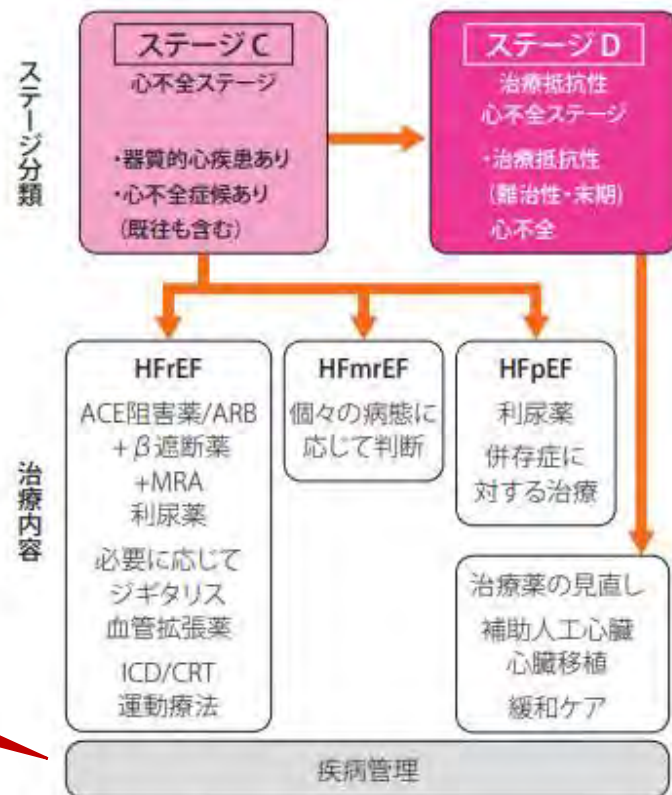


図10 心不全治療アルゴリズム



2021年 JCS/JHFS ガイドライン フォーカスアップデート版 急性・慢性心不全診療

JCS/JHFS 2021 Guideline Focused Update on Diagnosis and Treatment of Acute and Chronic Heart Failure

「急性・慢性心不全診療ガイドライン（2017年改訂版）」からあらたな知見をまとめ、フォーカスアップデートとして作成した。

疾病管理/運動療法/緩和ケア
≡心臓リハビリテーションは

すべてに対して上流に位置づけられ、
薬物療法選択前の前提

心臓リハビリテーションは
特殊な対象に、
特殊な環境で行われる、ものではなく
目の前の心疾患患者全員が対象
(保険請求は別)

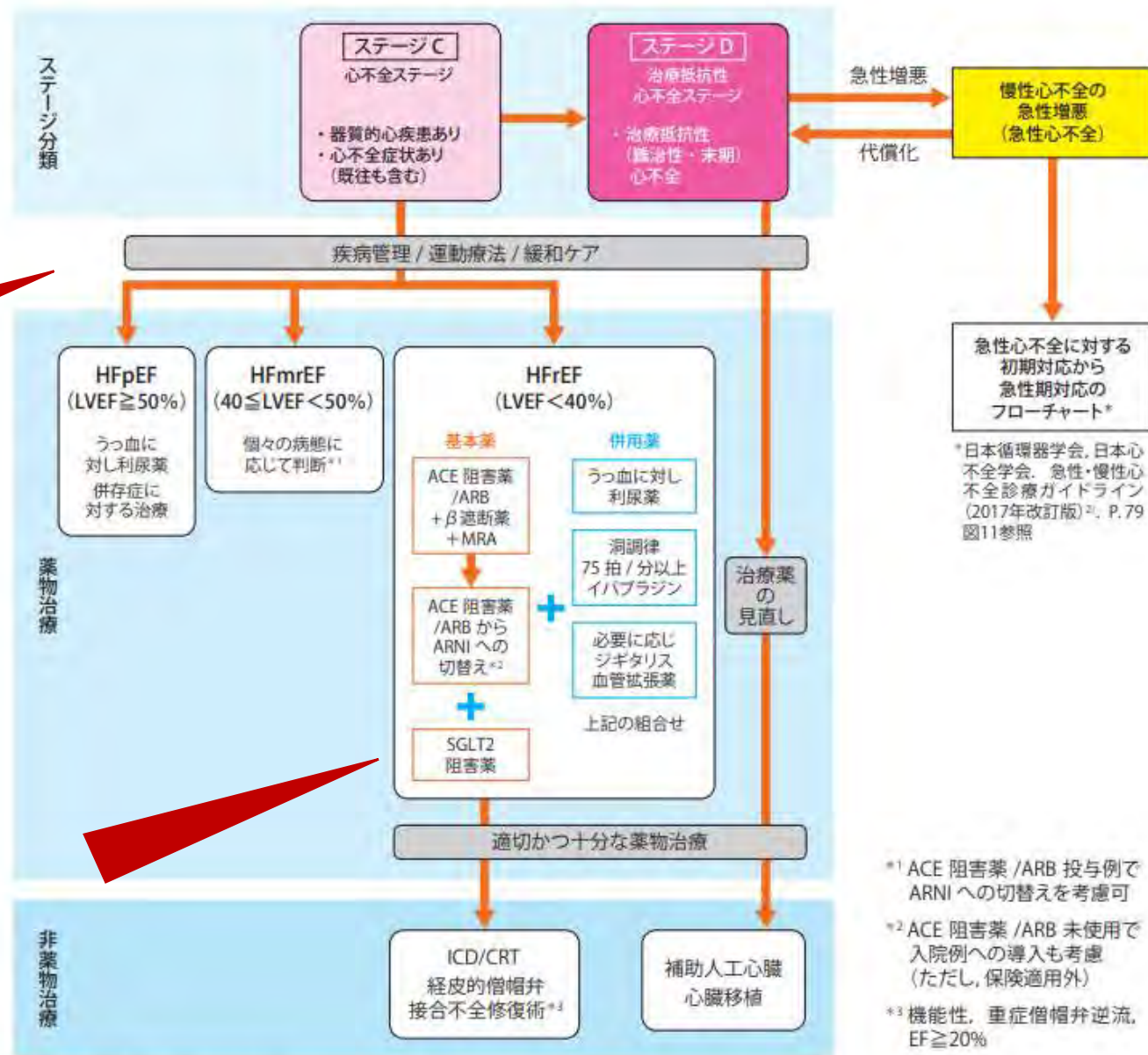


図 2 心不全治療アルゴリズム



変わった診療報酬



⑤リハビリテーション等の取組

(現状・課題)

循環器病患者においては、社会復帰という観点も踏まえつつ、日常生活動作の向上等の生活の質の維持向上を図るため、早期からの継続的なリハビリテーションの実施が必要となる場合もある。

脳卒中患者では、急性期診療を行った後も様々な神経症状が残ることが多い。

一般的には、急性期に速やかにリハビリテーションを開始し、円滑に回復期及び維持期のリハビリテーションに移行することが求められ、医療と介護の間で切れ目のない継続的なリハビリテーションの提供体制をより一層構築していく必要がある。リハビリテーションと同時に合併症の治療が必要な場合や合併症の治療が優先される場合もあり、個々の患者に応じた適切な対応が求められる。また、患者がその目的や必要性を十分に理解した上での再発予防、重症化予防、生活再建や就労等を目的とした多職種によるアプローチが重要である。

心血管疾患患者の管理においては、特に、心不全等で入退院を繰り返す患者が増加しており、再発予防及び再入院予防の観点が重要である。運動療法、冠危険因子是正、患者教育、カウンセリング等を含む多職種による疾病管理プログラムとして心血管疾患におけるリハビリテーションを実施することが関連学会より提唱されている。



特に心不全等で入退院を繰り返す患者が増加しており、再発予防及び再入院予防の観点が重要



Disease Management and Outcomes in Patients Hospitalized for Acute Heart Failure in Japan

Lei Chen · Raluca Ionescu-Iltis · Helel Romdhani · Annie Guerin ·
Paul Kissler · Maria Boncinini · Keith Tinead · Mary DeSouza ·
Naoki Sato

急性心不全入院治療の実態の推移 →急性期病床のみでは完結しない

DPC II超過

220

Cardiol Ther (2021) 10:211–228

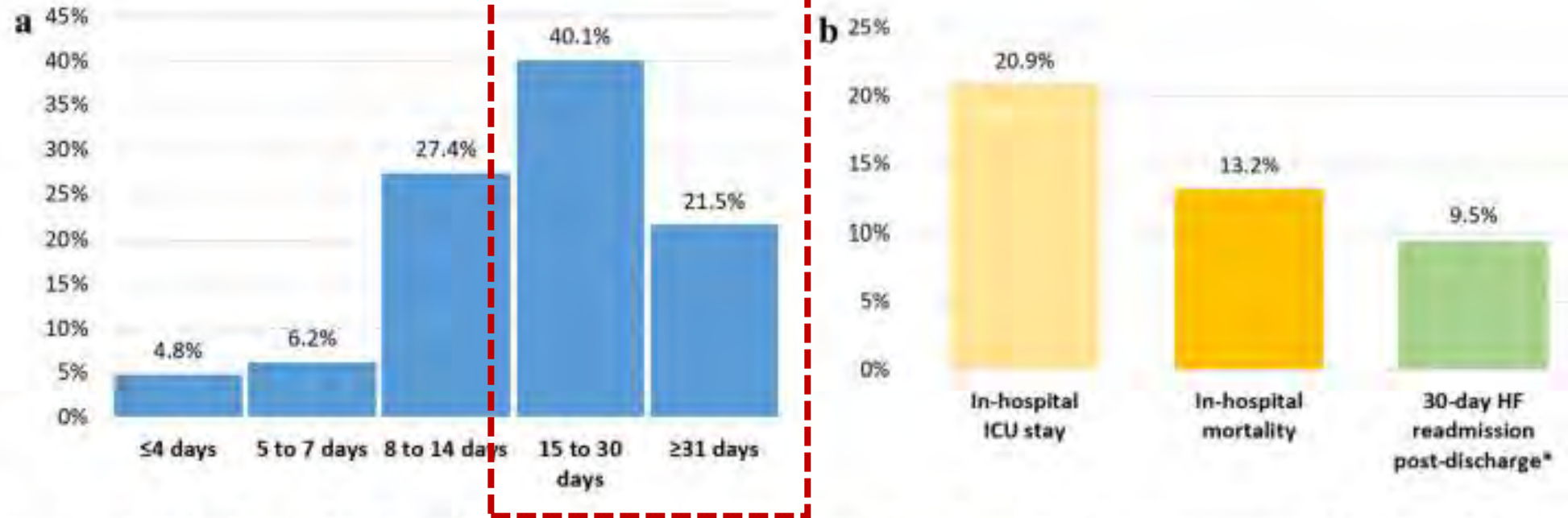


Fig. 1 **a** Length of stay for the index hospitalization. **b** In-hospital and post-discharge outcomes. *HF* heart failure, *ICU* intensive care unit. *Asterisk* indicates estimated among patients discharged alive



急性期病院では良いアウトカムを目指す

早期にしっかりうっ血解除、eGFR維持

Clinical course and predictive value of congestion during hospitalization in patients admitted for worsening signs and symptoms of heart failure with reduced ejection fraction: findings from the EVERSET trial.

Eur Heart J 2013;34:835-843

Clinical Effectiveness of Tolvaptan in Patients With Acute Heart Failure and Renal Dysfunction

J Card Fail 2016 ; 22:423-432.

身体活動保持（HAD防止）、**早期のリハ（ ≤ 3 日）** 介入

Predictive impact of early mobilization on rehospitalization for elderly Japanese heart failure patients

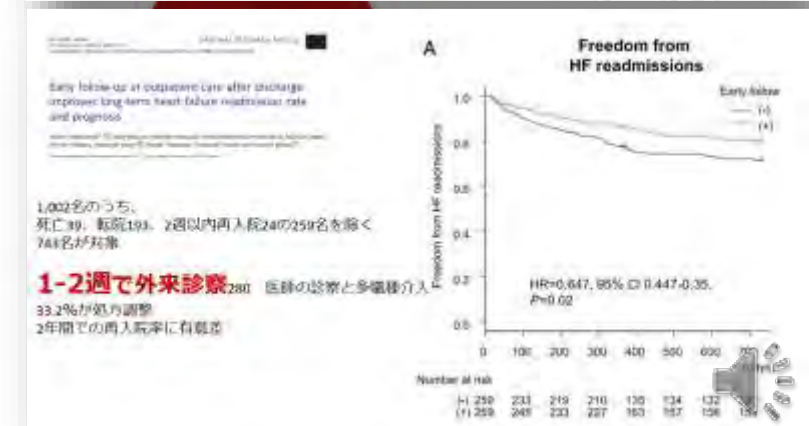
Heart and Vessels 2020;35:531-536

疾病管理、継続リハ、社会的支援への**確実な連携**

退院後**早期（ $\leq 7-14$ 日）**の外来受診確認後に逆紹介

Early follow-up at outpatient care after discharge improves long-term heart failure readmission rate and prognosis

ESC Heart Fail 2021;8:3002-3013



SPECIAL REPORT

Rehospitalization for Heart Failure

Predict or Prevent?

Akshay S. Desai, MD, MPH and Lynne W. Stevenson, MD

Division of Cardiovascular Quality and Outcomes



極早期からの訪問看護導入

High-Value Home Health Care for Patients With Heart Failure

An Opportunity to Optimize Transitions From Hospital to Home

Christine C. Jones, MD, MSc, Sarah J. D'Amico, PhD, RN, Angelika Kozminski, PhD, RN, Rebecca C. Russell, MD, PhD, and Peppino A. Moschetti, MD, MSc

Health Serv Res. doi: 10.1111/1475-6773.12537.

combination of early and intensive HHC combined with an outpatient clinician visit within the first 7 days after hospital discharge were significantly less likely to be readmitted to the hospital within 30 days.

≥1 HHC nursing visits within 1 day of hospital discharge for a total of ≥3 visits in the first week after discharge

J Healthc Qual. 2011;33:17-23.

combination of formalized communication between hospital, HHC, and outpatient clinicians; primary care follow-up within 7 days; and frontloading of HHC visits had a lower odds of 30-day hospital readmissions compared with a control group receiving usual care (adjusted odds ratio: 0.57 [95% confidence interval, 0.38-0.87]).

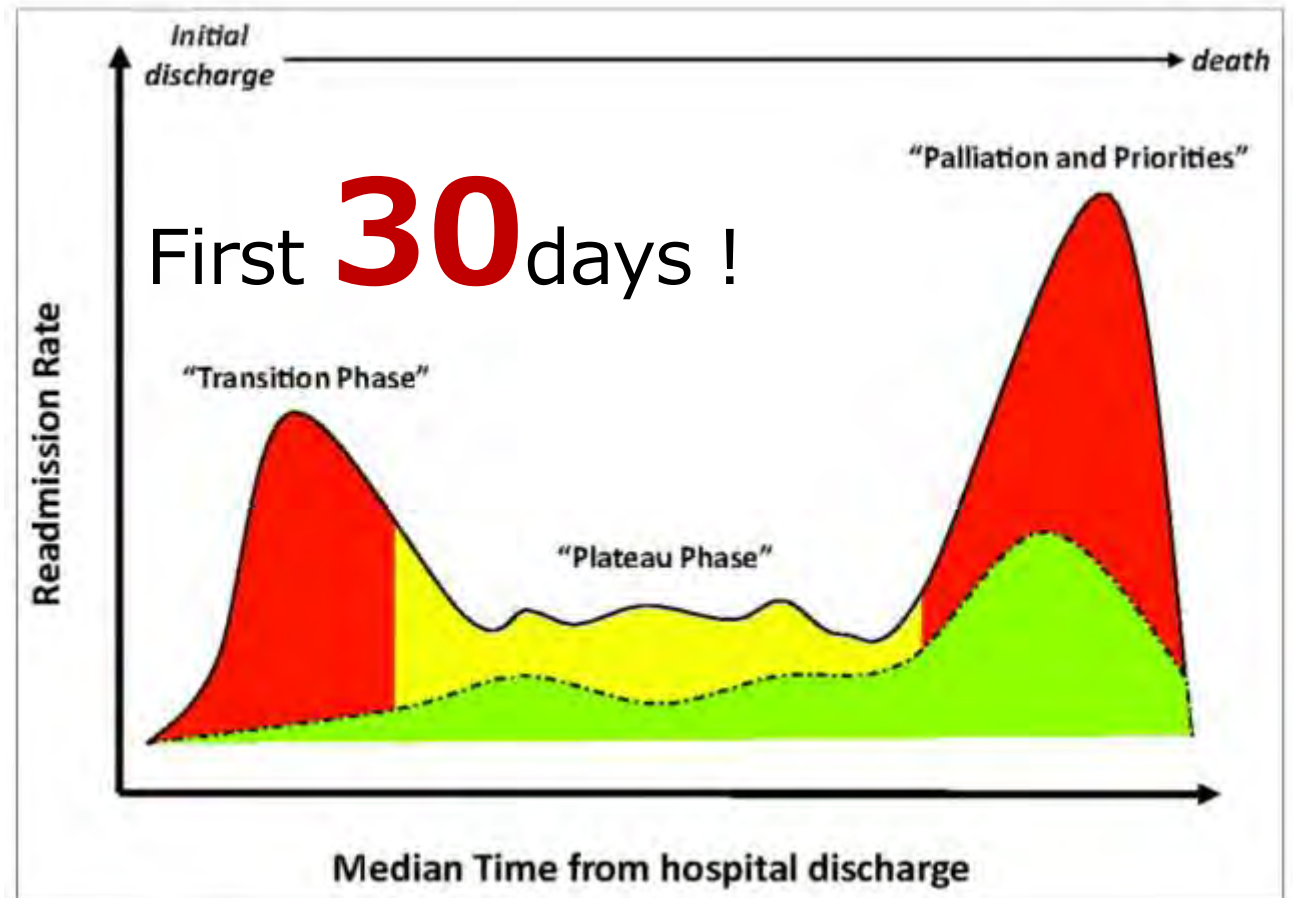
再入院減
再入院が軽症、入院期間と医療費減
体重、食事、服薬見守り、孤立防止

Figure 1. Three-phase terrain of lifetime readmission risk after heart failure hospitalization. Figure drawn to schematically depict data from Chun et al.⁷ and Russo et al.¹⁹ The shaded red areas depict periods of highest risk for readmission immediately following discharge and just before death; the shaded yellow area reflects the lower risk plateau phase; and the shaded green reflects the assumed baseline of unavoidable readmissions.

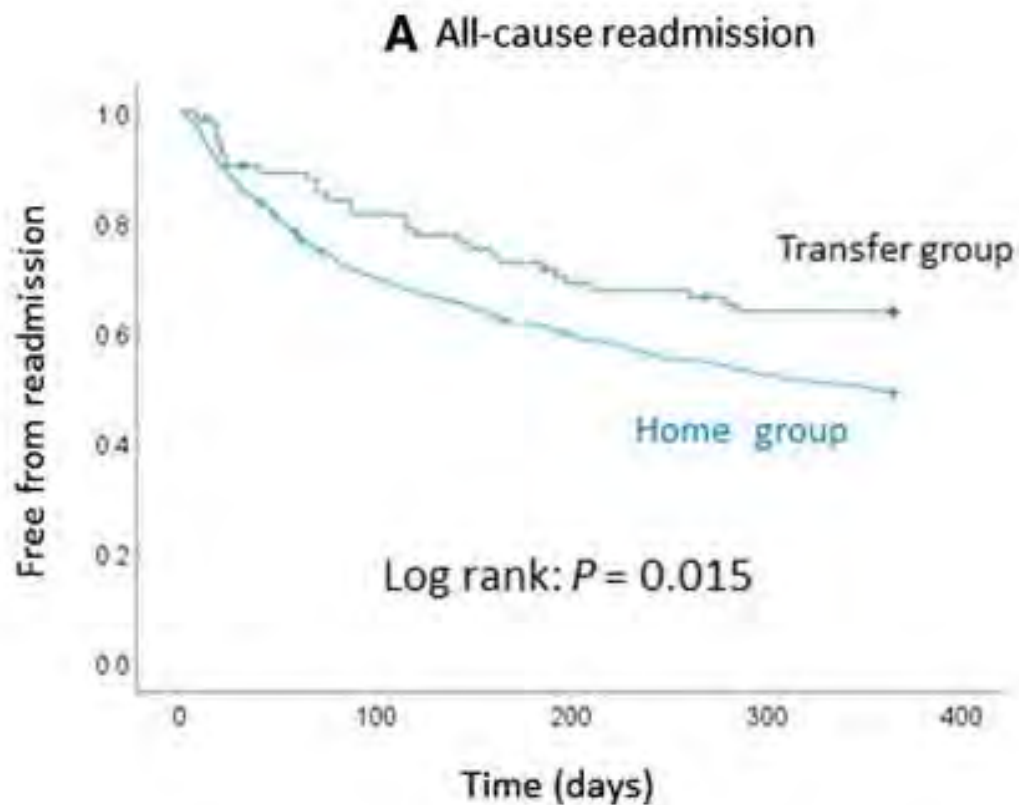




Discharge disposition and 1-year readmission in acute-phase hospitalized patients with heart failure: a retrospective observational multi-center study

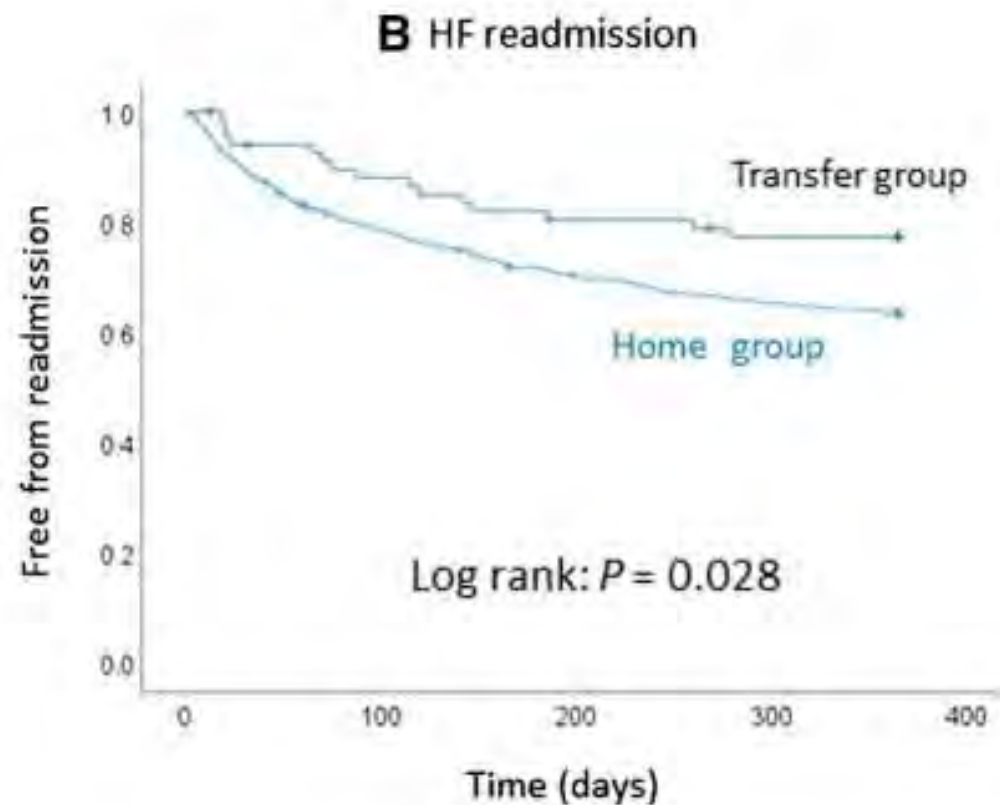
Michitaka Kato¹ · Yuji Mori² · Daisuke Watanabe³ · Hiroshige Onoda⁴ · Keita Fujiyama⁵ · Masahiro Toda⁶ · Kazuya Kito²

Received: 29 November 2021 / Accepted: 11 March 2022
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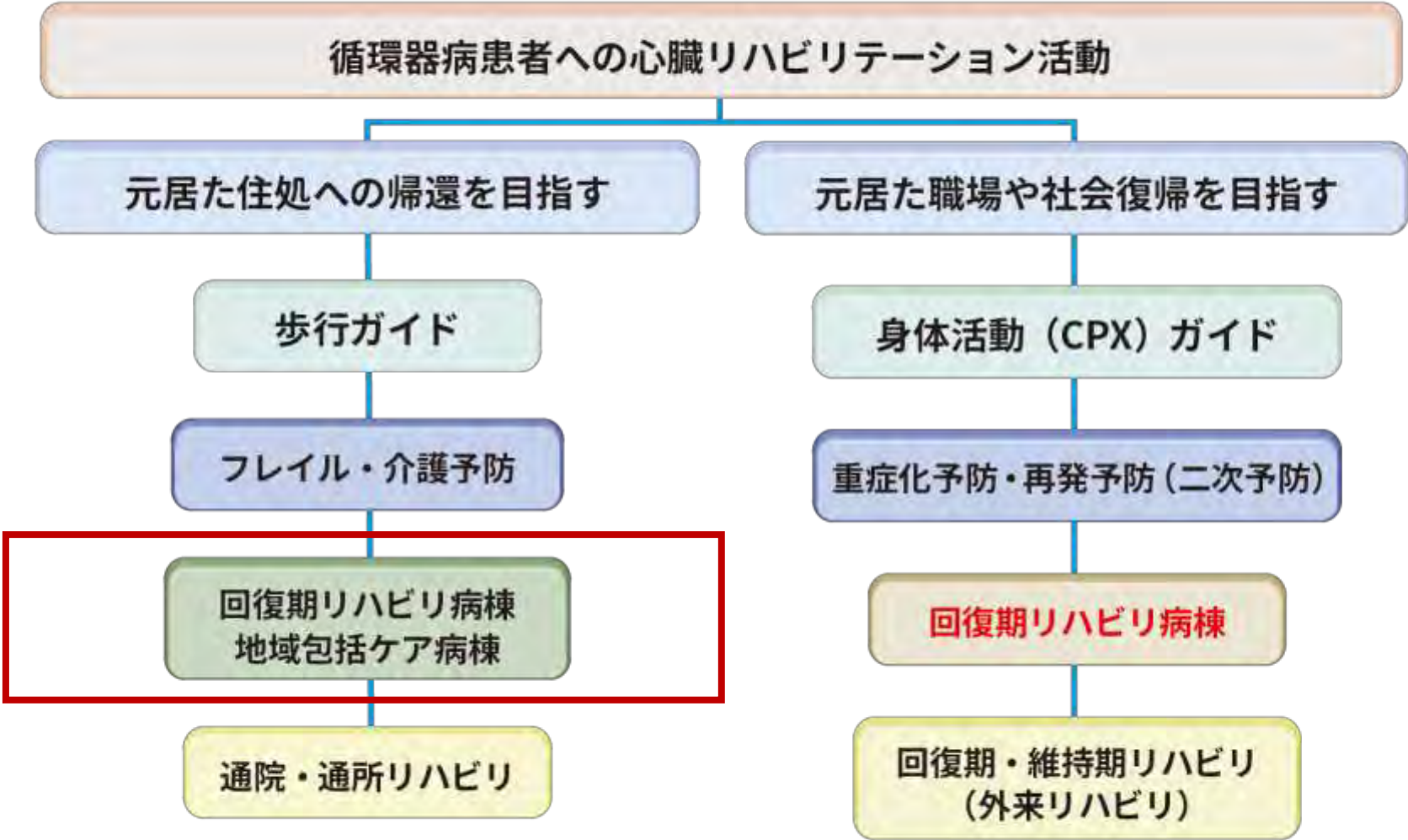


BI<60は再入院多い

自宅退院より転院の方が
1年後の全再入院、心不全再入院少
全死亡には差はなし



循環器病患者への心臓リハビリテーション活動



転院リハと
いう選択肢

社会資源を活用する。	I	A	A	I
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回復期リハビリテーション病棟入院料に係る見直し

回復期リハビリテーションを要する状態の見直し

- 回復期リハビリテーションを要する状態について、「急性心筋梗塞、狭心症発作その他急性発症した心大血管疾患又は手術後の状態」を追加し、算定上限日数を90日以内とする。

	回復期リハビリテーションを要する状態	算定上限日数
回復期リハビリテーション病棟入院料に入院する患者	1 脳血管疾患、脊髄損傷、頭部外傷、くも膜下出血のシャント手術後、脳腫瘍、脳炎、急性脳症、脊髄炎、多発神経炎、多発性硬化症、腕神経叢損傷等の発症後若しくは手術後の状態又は義肢装着訓練を要する状態	○ 算定開始日から起算して 150日以内 ○ 高次脳機能障害を伴った重症脳血管障害、重度の頸髄損傷及び頭部外傷を含む多部位外傷の場合は、算定開始日から起算して 180日以内
	2 大腿骨、骨盤、脊椎、股関節若しくは膝関節の骨折又は2肢以上の多発骨折の発症後又は手術後の状態	○ 算定開始日から起算して 90日以内
	3 外科手術後又は肺炎等の治療時の安静により廃用症候群を有しており、手術後又は発症後の状態	○ 算定開始日から起算して 90日以内
	4 大腿骨、骨盤、脊椎、股関節又は膝関節の神経、筋又は靭帯損傷後の状態	○ 算定開始日から起算して 60日以内
	5 股関節又は膝関節の置換術後の状態	○ 算定開始日から起算して 90日以内
	(新) 6 急性心筋梗塞、狭心症発作その他急性発症した心大血管疾患又は手術後の状態	○ 算定開始日から起算して 90日以内



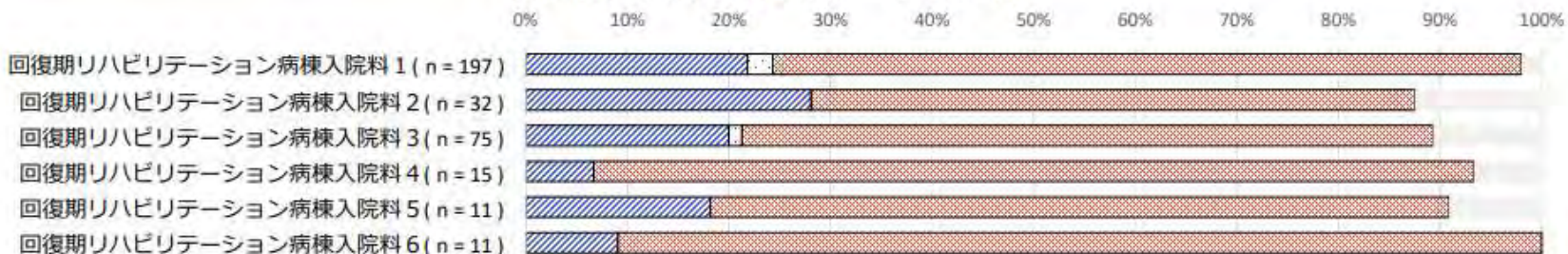
疾患別リハビリテーション料の届出状況①

診調組 入-1-1
3.6.16(改)

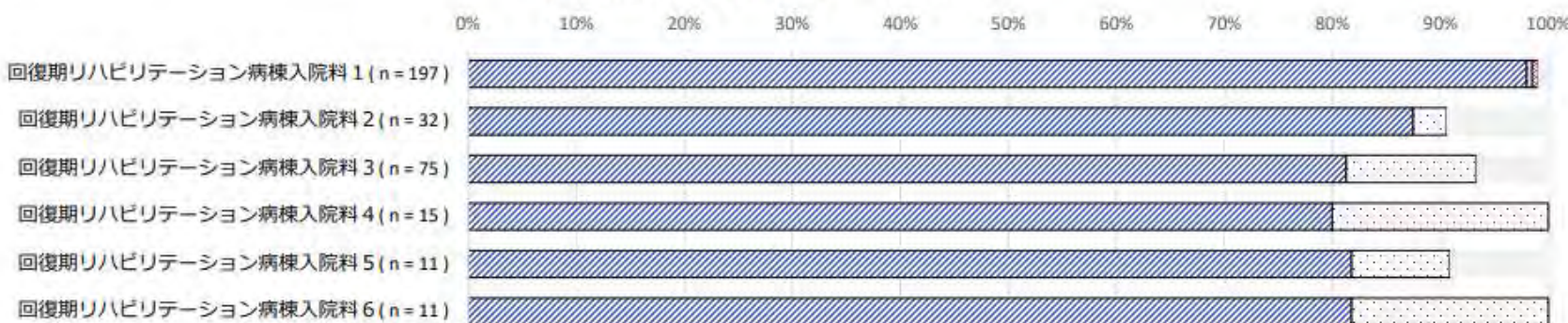
- 回復期リハビリテーション病棟入院料を届け出ている医療機関における、疾患別リハビリテーション料の届出状況は以下のとおりであった。
- 心大血管疾患リハビリテーション料を届け出ている医療機関が一定程度存在した。

回リハ1でも
せいぜい
4分の1の
届出状況

心大血管疾患リハビリテーション料



脳血管疾患リハビリテーション料



KNOW THE RULES!



急性心不全は 対象？
慢性心不全急性増悪は 対象？

要確認

「急性発症した心大血管疾患」とは

ア 急性発症した心大血管疾患又は心大血管疾患の手術後の患者とは、急性心筋梗塞、狭心症、開心術後、経カテーテル大動脈弁置換術後、大血管疾患（大動脈解離、解離性大動脈瘤、大血管術後）のものをいう。

[特掲診療料の施設基準等別表第九の四に掲げる対象患者](#)



演者の個人的見解

フレイル心不全の急性期後 地ケア病棟？

リハ<在宅復帰支援

HADによる在宅復帰への支障を解消

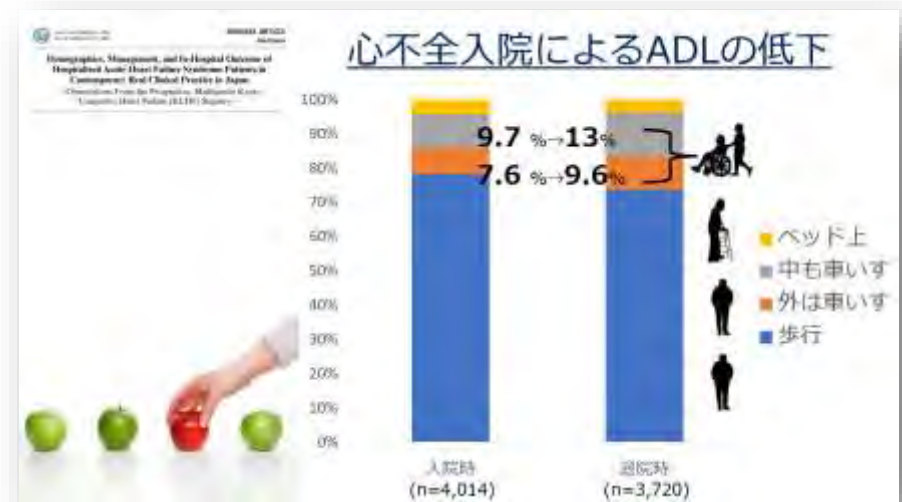
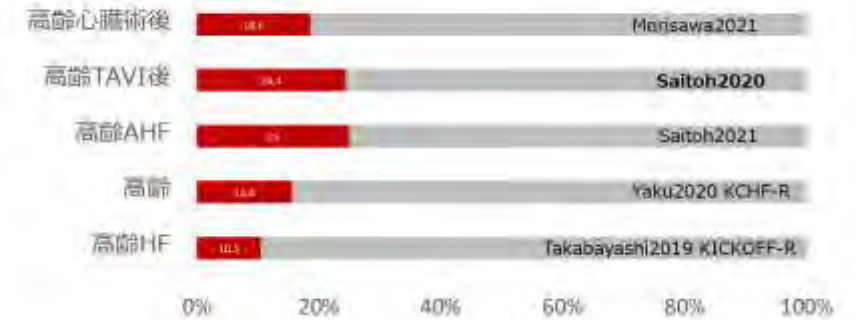
達成目標確認、リハによるADL向上

介護保険サービス調整

家族支援 Caregiver教育



本邦高齢心疾患患者のHAD頻度



演者の個人的見解



地ケア病棟 院内転棟比率 \geq 6割で減算

院内転棟で完結ではなく
地域での病病連携も視野



地域における包括ケアネットワーク



地域心臓リハビリテーション



「**地域ぐるみ**で取り組む」 JMAPスピリットそのもの!!

当学会は、各地で高齢者を支える地域包括ケア&ケアを、**地域ぐるみの連携協働**により進めようとするヘルスケア関係者並びに関連企業の英知と知見を結集し、高齢者の医療・介護の重症化予防システムの構築とそれを担う人材の育成を図り、公益の増進に寄与することを目指しています。





やわたメディカルセンター
YAWATA MEDICAL CENTER
病気にならないための病院



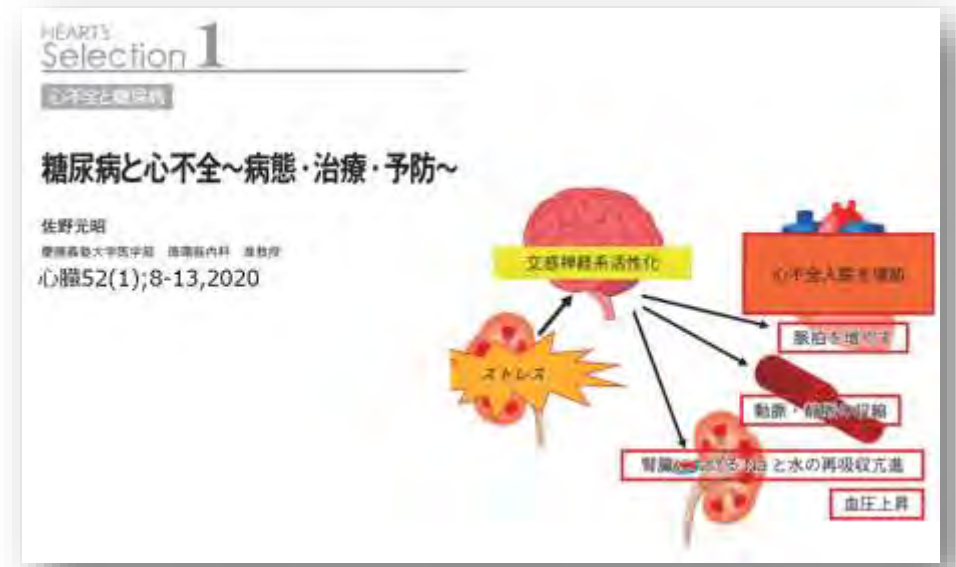
心不全と糖尿病

糖尿病患者の初回入院理由は心不全

非糖尿病に比し、糖尿病では発症率高い（男性2倍、女性5倍）

糖尿病コントロールが悪いと心不全合併率が高い

糖尿病患者の心不全合併率は高くなっている（1989年13% 1999年47%）

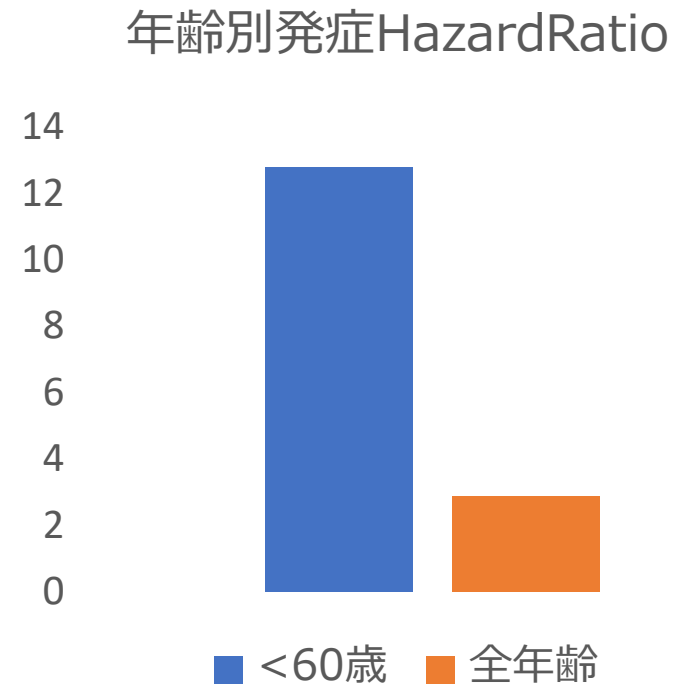
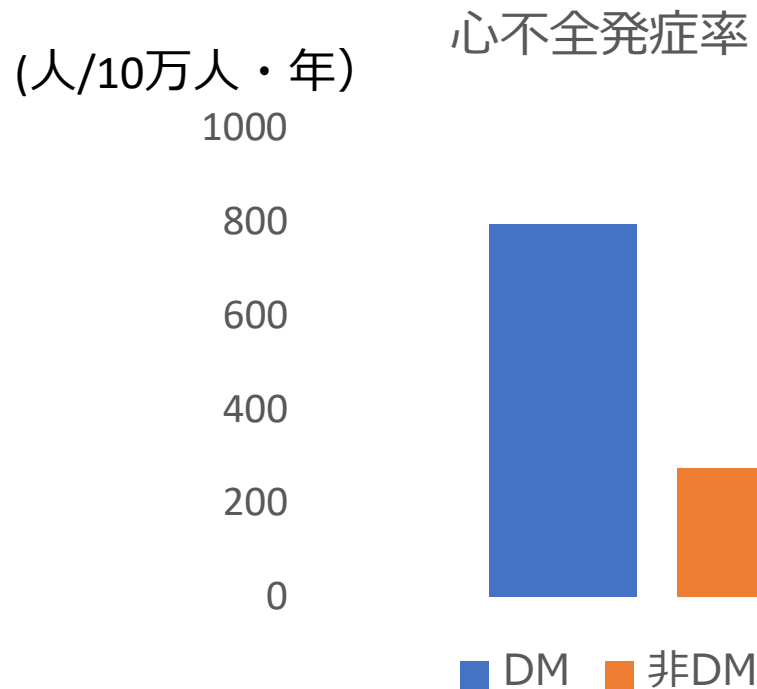


心不全と糖尿病

糖尿病患者の**50%**は心不全を発症

糖尿病と心不全の両方を有する患者の方がより重篤な転帰

J Card Fail. 2009 Mar; 15(2):152-7.

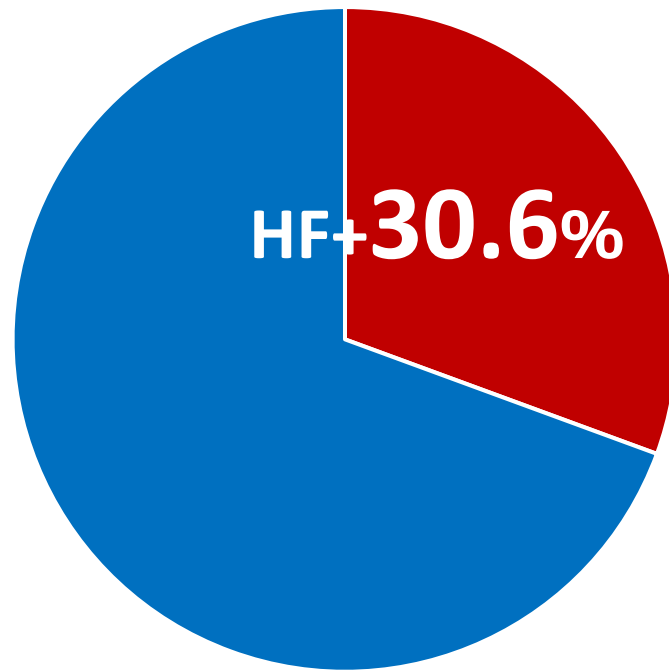


心不全と糖尿病

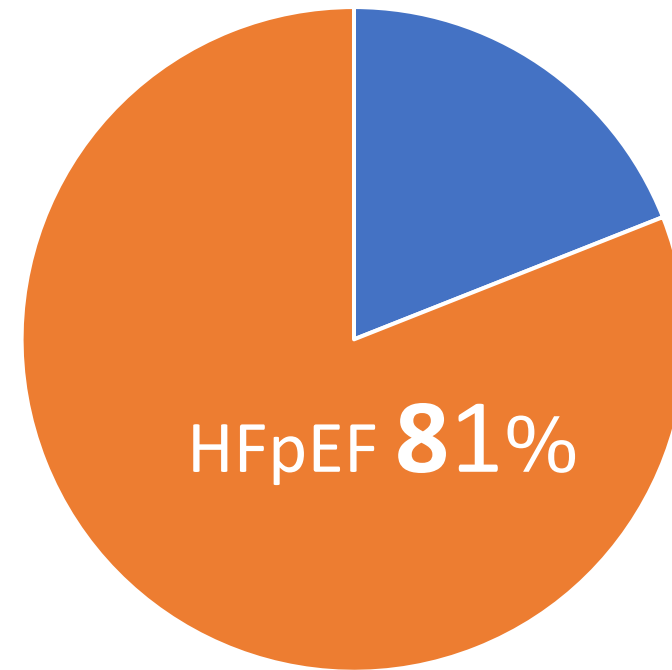
糖尿病患者の心不全の8割はHFpEF

Diabetologia 2012;55:2154

心不全有病率



病態



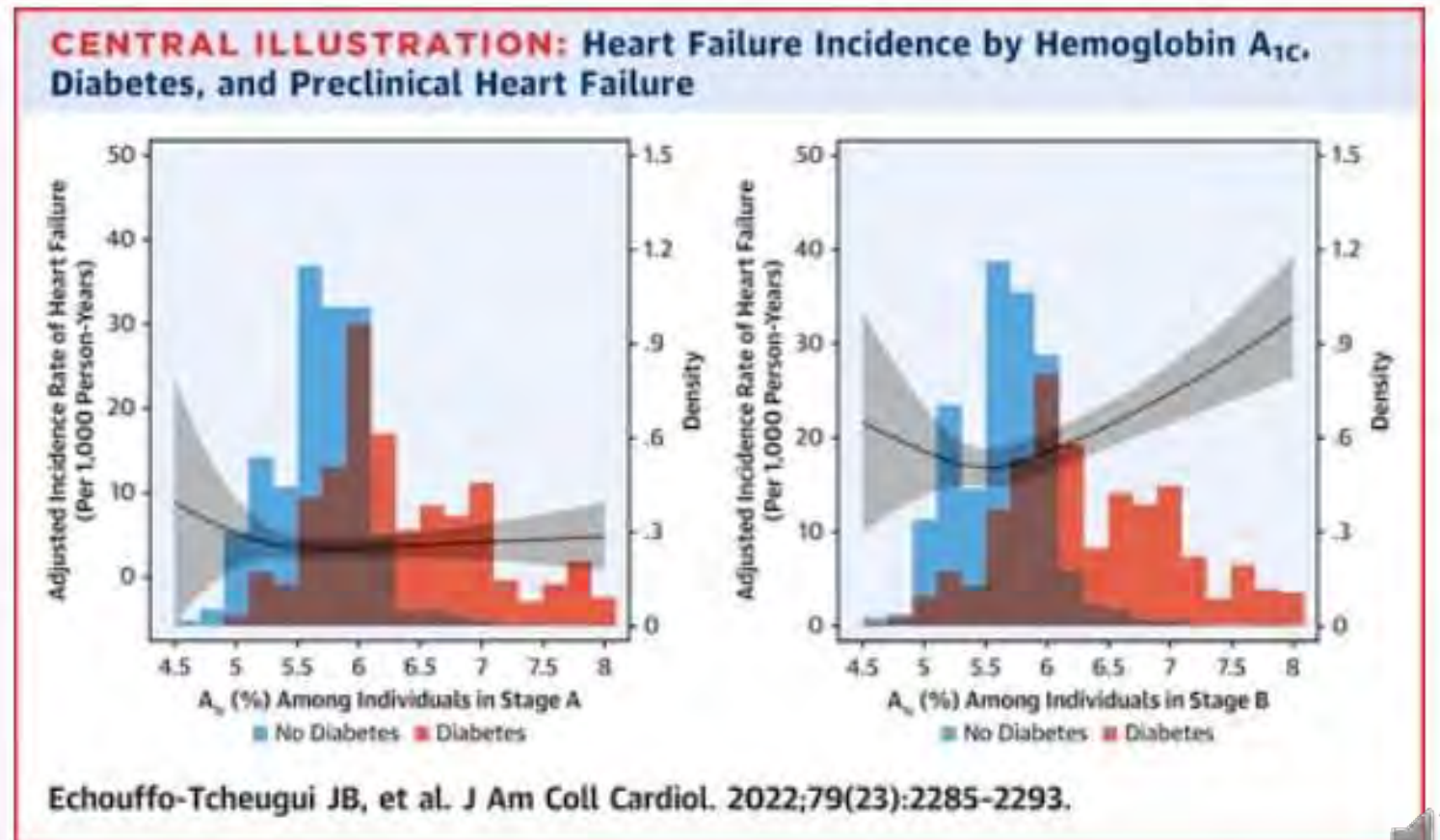
血糖コントロールは重要

血糖管理不良の糖尿病は心不全への進行リスクが高い——ARIC研究 ステージBではHbA1c7%以上でハイリスク

8.6年の追跡期間中に470件の心不全イベントが発生。
ステージBでHbA1c7%以上の糖尿病群は、HbA1c7%未満の糖尿病群または非糖尿病群に比較し、より若年で症候性心不全へ進行。

ステージB〔HR1.83（同1.33～2.51）〕では有意な関連。

ステージBでHbA1c7%以上の群は、ステージAの非糖尿病群に比較し、症候性心不全リスクが**7倍以上高かった**。
〔HR7.56（同4.68～12.20）〕

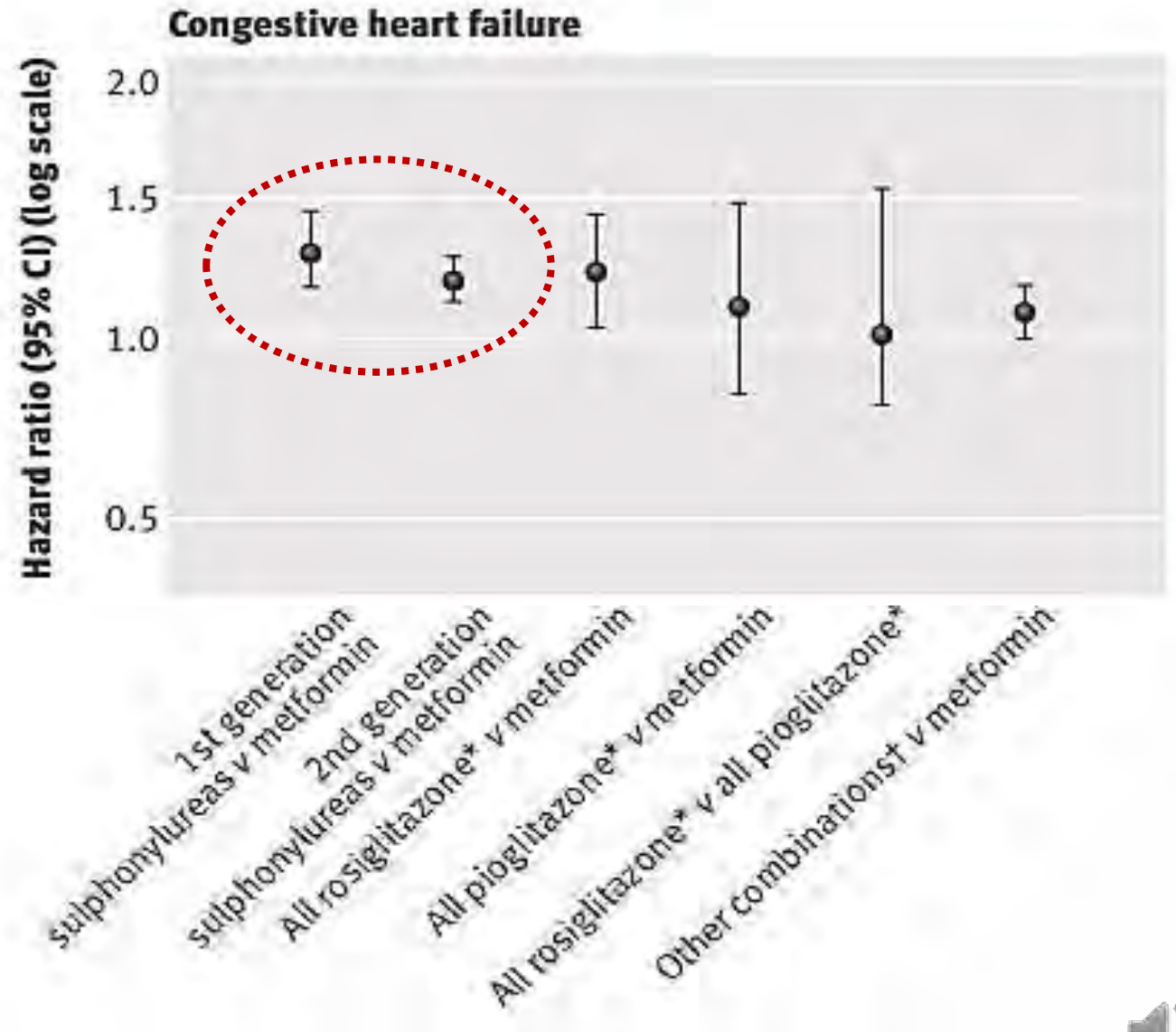


Risk of cardiovascular disease and all cause mortality among patients with type 2 diabetes prescribed oral antidiabetes drugs: retrospective cohort study using UK general practice research database

Ioanna Tzoulaki, lecturer,¹ Mariam Molokhia, senior lecturer,² Vasa Curcin, research associate,³ Mark P Little, reader,⁴ Christopher J Millett, senior lecturer in public health,⁵ Anthea Ng, research associate,⁶ Robert I Hughes, research associate,⁷ Kamlesh Khunti, professor,⁸ Martin R Wilkins, professor,⁹ Azeem Majeed, professor,⁹ Paul Elliott, professor¹⁰

Cite this as: *BMJ* 2009;339:b4731
doi:10.1136/bmj.b4731

メトホルミンと比較
SU剤では心不全リスク高い



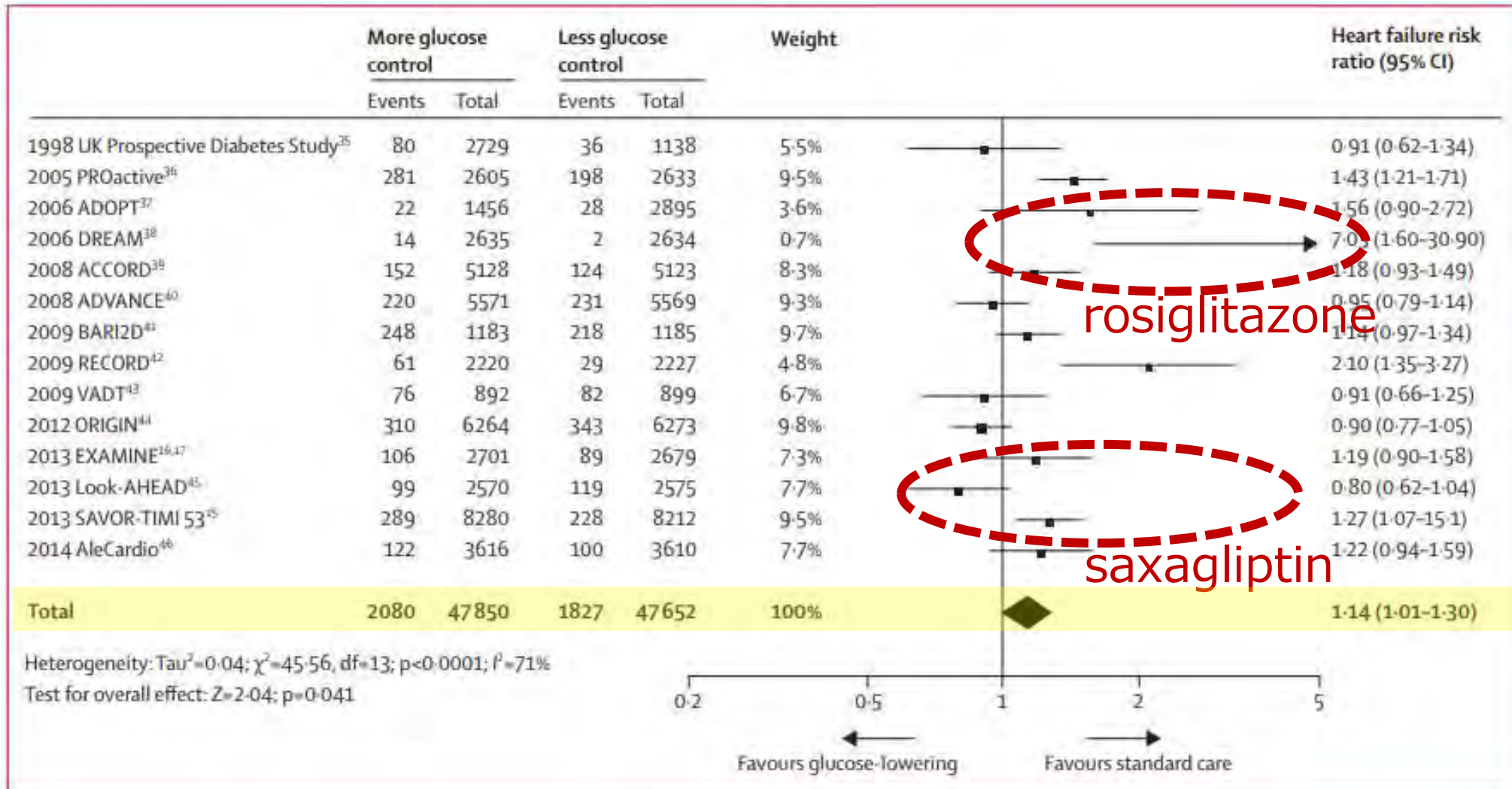


Glucose-lowering drugs or strategies and cardiovascular outcomes in patients with or at risk for type 2 diabetes: a meta-analysis of randomised controlled trials

Lancet Diabetes Endocrinol
2015; 3: 356-66

Jacob A Udell, Matthew A Cavender, Deepak L Bhatt, Saurav Chatterjee, Michael E Farkouh, Benjamin M Scirica

薬による
心不全リスクに
違いあり



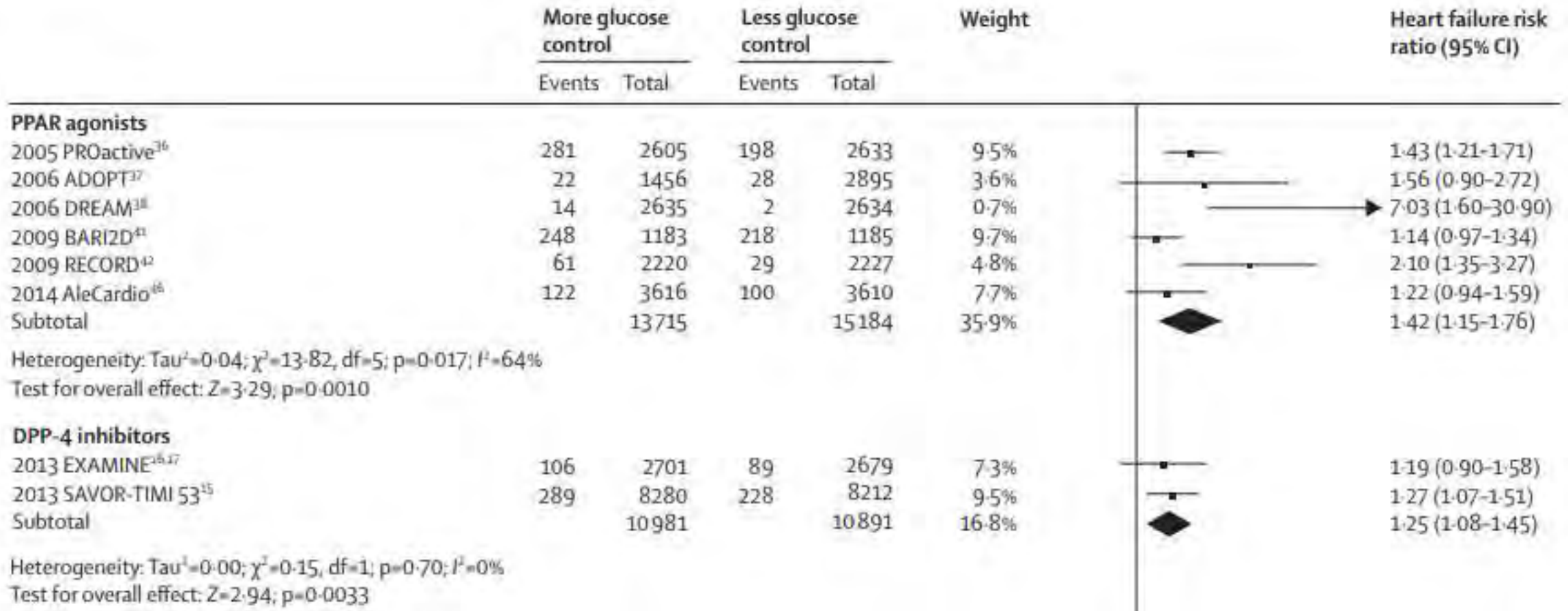


Glucose-lowering drugs or strategies and cardiovascular outcomes in patients with or at risk for type 2 diabetes: a meta-analysis of randomised controlled trials

Lancet Diabetes Endocrinol
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Jacob A Udell, Matthew A Cavender, Deepak L Bhatt, Saurav Chatterjee, Michael E Farkouh, Benjamin M Scirica

チアゾリジン系
一部のDPP-IVi
第2世代SU
(メトホルミン)



心不全：糖尿病のあまり認識されていない独立した合併症

1670

Diabetes Care Volume 45, July 2022



Heart Failure: An Underappreciated Complication of Diabetes. A Consensus Report of the American Diabetes Association

Rodica Pop-Busui,¹ James L. Januzzi,²
Dennis Bruemmer,³ Sonia Butalia,⁴
Jennifer B. Green,⁵ William B. Horton,⁶
Colette Knight,⁷ Moshe Levi,⁸
Neda Rasouli,⁹ and
Caroline R. Richardson¹⁰

Diabetes Care 2022;45:1670–1690 | <https://doi.org/10.2337/dci22-0014>





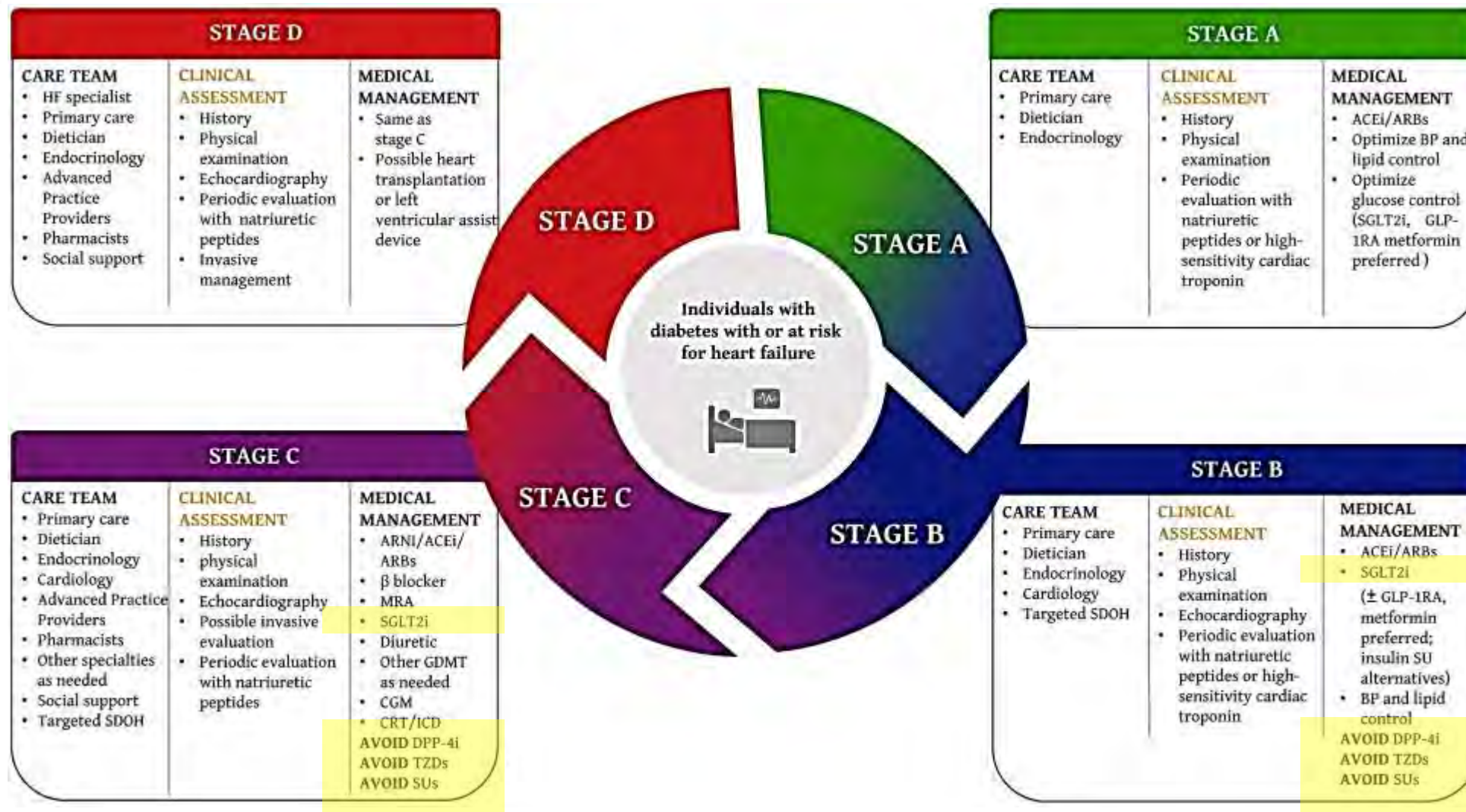
Heart Failure: An Underappreciated Complication of Diabetes. A Consensus Report of the American Diabetes Association

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Radica Pop-Busui,¹ James L. Januzzi,²
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Colette Knight,⁷ Moshe Levi,⁸
Neda Rasouli,⁹ and
Caroline R. Richardson¹⁰

ステージ別マネジメントにおける薬物選択





Heart Failure: An Underappreciated Complication of Diabetes. A Consensus Report of the American Diabetes Association

Diabetes Care 2022;45:1670–1690 | <https://doi.org/10.2337/dci22-0014>

Radica Pop-Busui,¹ James L. Januzzi,² Dennis Bruemmer,³ Sonia Butalia,⁴ Jennifer B. Green,⁵ William B. Horton,⁶ Colette Knight,⁷ Moshe Levi,⁸ Neda Rasouli,⁹ and Caroline R. Richardson¹⁰

顕性心不全となる**前**から
SGLT2iを選び
DPP-IVi
TZDs
SUs を回避する

STAGE B		
CARE TEAM <ul style="list-style-type: none"> • Primary care • Dietician • Endocrinology • Cardiology • Targeted SDOH 	CLINICAL ASSESSMENT <ul style="list-style-type: none"> • History • Physical examination • Echocardiography • Periodic evaluation with natriuretic peptides or high-sensitivity cardiac troponin 	MEDICAL MANAGEMENT <ul style="list-style-type: none"> • ACEI/ARBs • SGLT2i (± GLP-1RA, metformin preferred; insulin SU alternatives) • BP and lipid control <p>AVOID DPP-4i AVOID TZDs AVOID SUs</p>



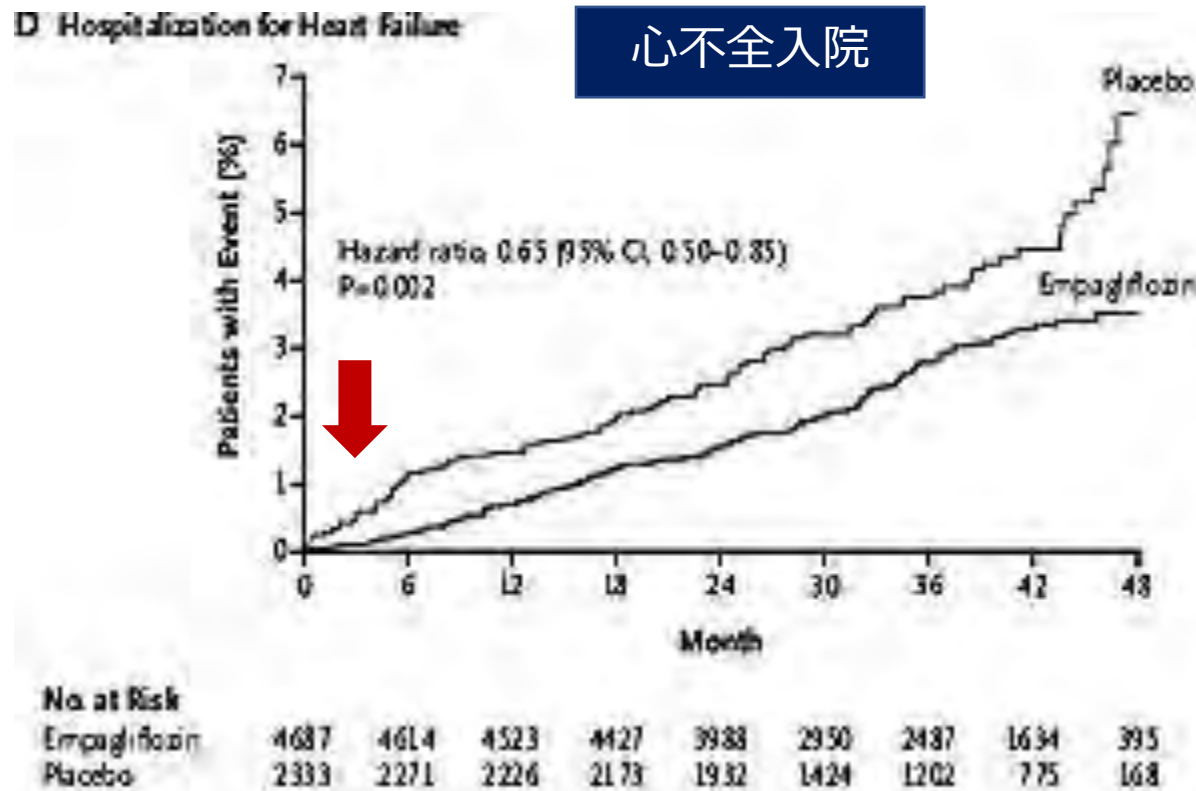
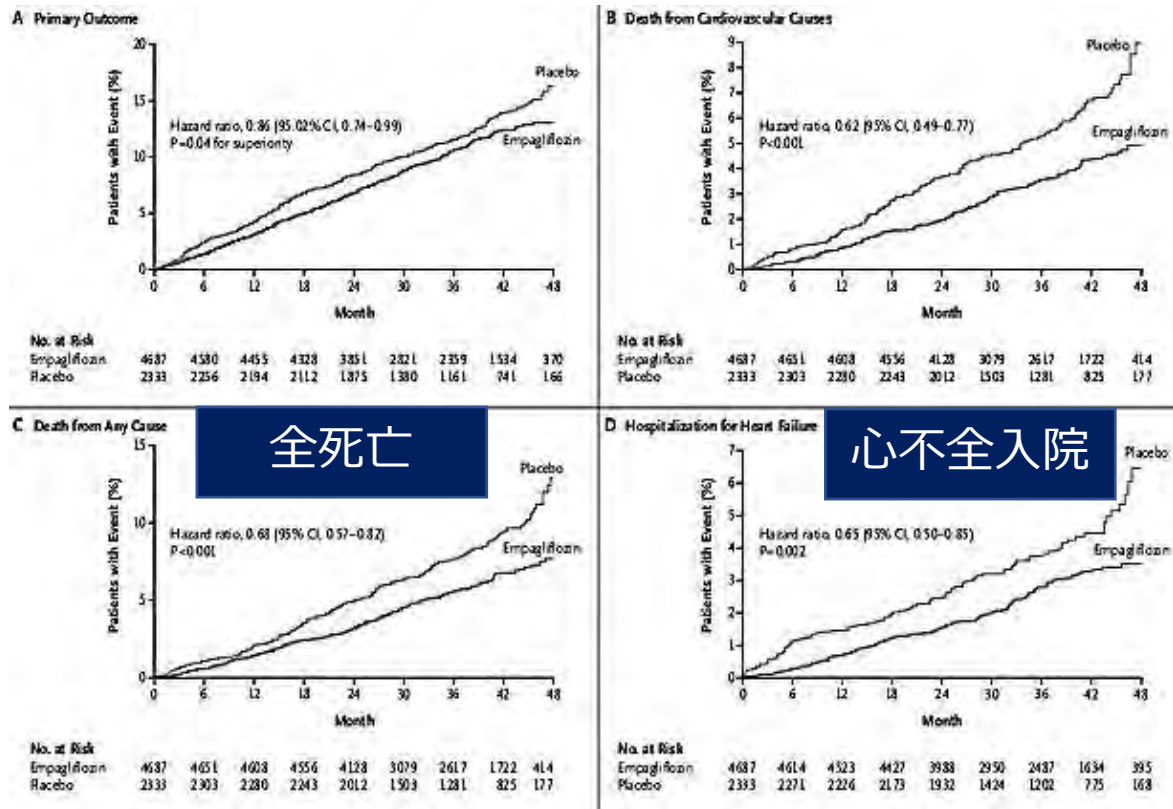
糖尿病治療新薬は
心不全を悪化させないか？



Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Bernard Zinman, M.D., Christoph Wanner, M.D., John M. Lachin, Sc.D., David Fitchett, M.D., Erich Bluhmli, Ph.D., Stefan Hantel, Ph.D., Michaela Matheis, Dipl. Biomat., Theresa Deviris, Dr. P.H., Odd Erik Johansen, M.D., Ph.D., Hans J. Woerle, M.D., Ulf C. Broedl, M.D., and Silvio E. Inzucchi, M.D., for the EMPA-REG OUTCOME Investigators

EMPA-REG-Outcome SGLT2iが糖尿病治療薬から「変わる」幕開け 再入院予防と予後には効果発現時期に差



心不全入院

全死亡

心不全入院



Sodium-glucose cotransporter 2 inhibitors' mechanisms of action in heart failure

Petra Grubić Rotkvić, Maja Cigrovski, Barbara Biloblić, Bilal Bulić, Luka Botić, Ivana Čelan

対象患者として心不全は1割程度**Table 1 Major cardiovascular outcome trials with sodium-glucose cotransporter 2 inhibitors**

Parameters	EMPA-REG OUTCOME	CANVAS program	DECLARE-TIMI 58
Intervention	Empagliflozin/placebo	Canagliflozin/placebo	Dapagliflozin/placebo
Median follow-up (yr)	3.1	3.6	4.2
Number of patients	7020	10142	17160
Prior cardiovascular disease/heart failure (%)	99/10	65.6/14.4	40/10
Primary outcome (3-point MACE)	0.86 (95%CI: 0.74-0.99) Noninferiority, $P < 0.001$; Superiority, $P = 0.04$	0.86 (95%CI: 0.75-0.97) Noninferiority, $P < 0.001$; Superiority, $P = 0.02$	0.93 (95%CI: 0.84-1.03) Noninferiority, $P < 0.001$; Superiority, $P = 0.17$
Cardiovascular death	0.62 (0.49-0.77) ¹	0.87 (0.72-1.06)	0.98 (0.81-1.17)
Myocardial infarction	0.87 (0.70-1.09)	0.89 (0.73-1.09)	0.89 (0.77-1.01)
Stroke	1.18 (0.89-1.56)	0.87 (0.69-1.09)	1.01 (0.84-1.21)
Heart failure hospitalization	0.65 (0.50-0.85) ¹	0.67 (0.52-0.87) ¹	0.73 (0.61-0.88) ¹
All cause mortality	0.68 (0.57-0.82) ¹	0.87 (0.74-1.01)	0.93 (0.82-1.04)

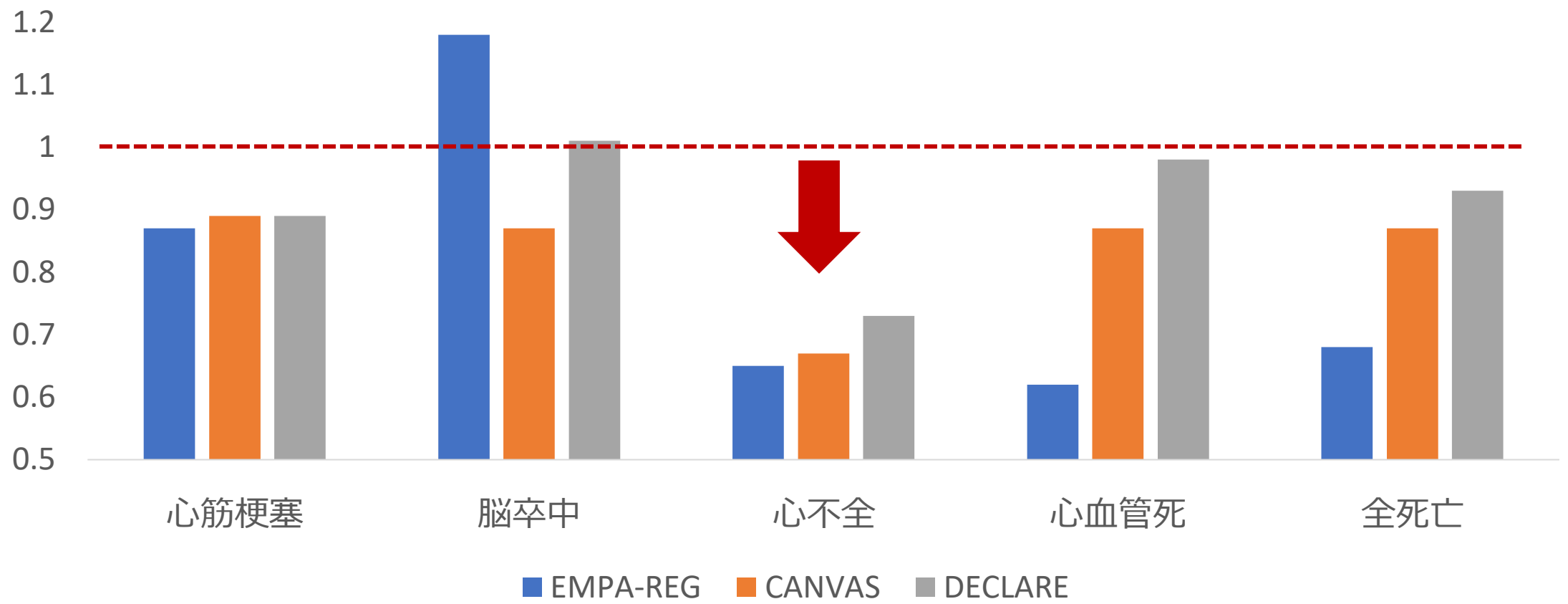


Sodium-glucose cotransporter 2 inhibitors' mechanisms of action in heart failure

Petra Grubić Rotkvić, Maja Cigrovski Berković, Nikola Bulj, Luka Rotkvić, Ivana Čelap

糖尿病患者を対象としたSGLT2阻害薬の大規模臨床試験における評価項目別ハザード比 (対象は偽薬群)

心不全30%、心血管死25%、非致死性心筋梗塞10%減、脳卒中不変

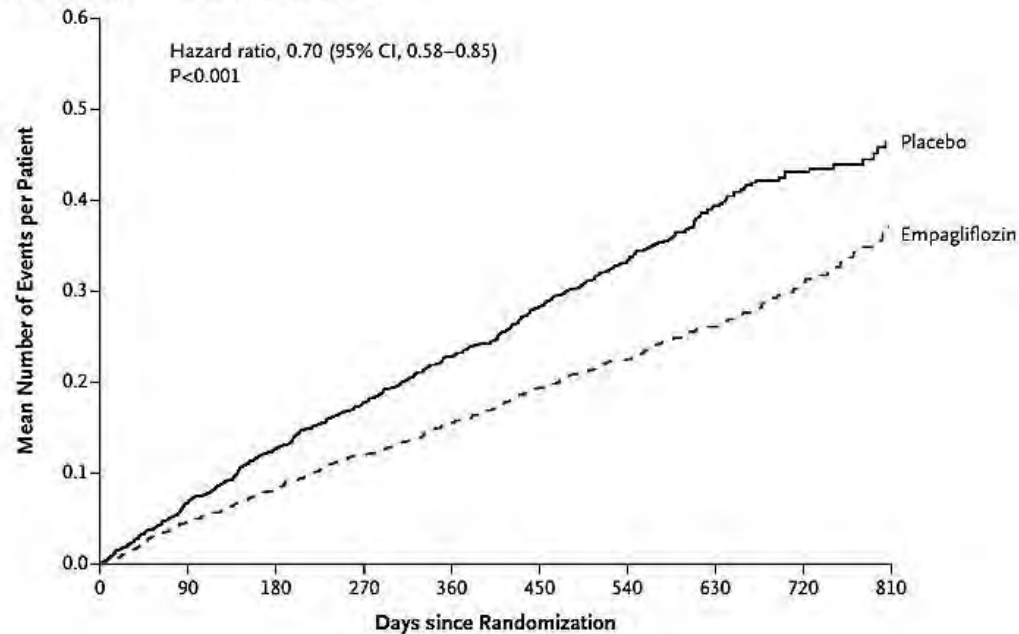


Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure

M. Packer, S.D. Anker, J. Butler, G. Filippatos, S.J. Pocock, P. Carson, J. Januzzi, S. Verma, H. Tsutsui, M. Brueckmann, W. Jamal, K. Kimura, J. Schnee, C. Zeller, D. Cottone, E. Bocchi, M. Böhm, D.-J. Choi, V. Chopra, E. Chuquilire, N. Giannetti, S. Janssens, J. Zhang, J.R. González-Juanatey, S. Kaul, H.-P. Brunner-La Rocca, B. Merkely, S.J. Nicholls, S. Perrone, I. Pina, P. Ponikowski, N. Sattar, M. Senni, M.-F. Seronde, J. Spinar, I. Squire, S. Taddei, C. Wanner, and F. Zannad, for the EMPEROR-Reduced Trial Investigators*

EMPEROR-**Reduced** 30%↓

B First and Recurrent Hospitalizations for Heart Failure

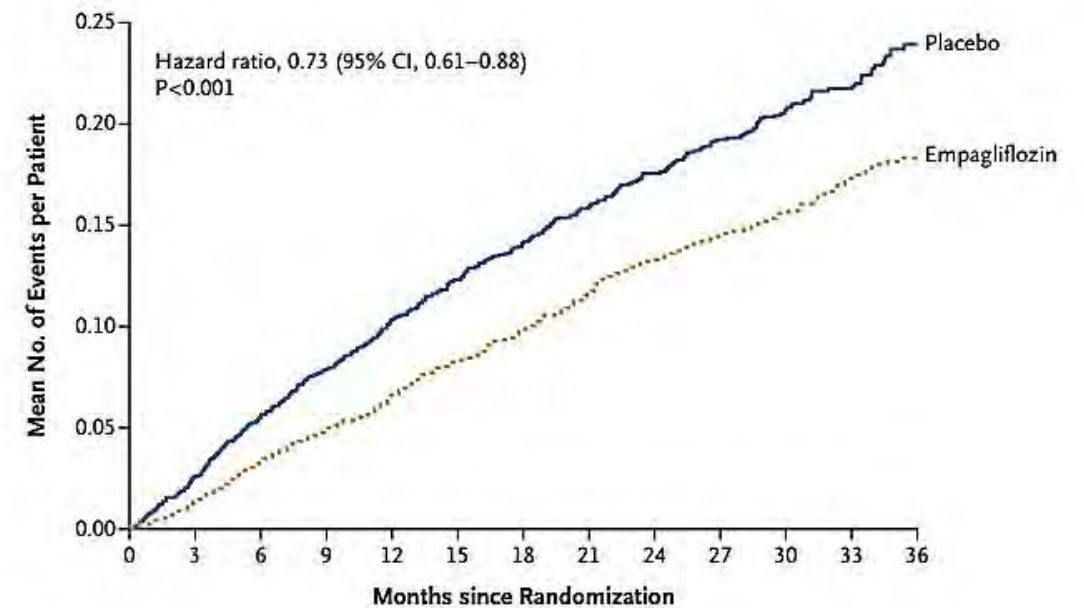


No. at Risk	0	90	180	270	360	450	540	630	720	810
Placebo	1867	1820	1762	1526	1285	1017	732	497	275	135
Empagliflozin	1863	1826	1768	1532	1283	1008	732	495	272	118

Empagliflozin in Heart Failure with a Preserved Ejection Fraction

S.D. Anker, J. Butler, G. Filippatos, J.P. Ferreira, E. Bocchi, M. Böhm, H.-P. Brunner-La Rocca, D.-J. Choi, V. Chopra, E. Chuquilire-Valenzuela, N. Giannetti, J.E. Gomez-Mesa, S. Janssens, J.-J. Januzzi, J.R. Gonzalez-Juanatey, B. Merkely, S.J. Nicholls, S.V. Perrone, I.L. Piña, P. Ponikowski, M. Senni, D. Spin, J. Spinar, I. Squire, S. Taddei, H. Tsutsui, S. Verma, D. Vineranu, J. Zhang, P. Carson, C.S.P. Lam, N. Marx, C. Zeller, N. Sattar, W. Jamal, S. Schneid, J.M. Schnee, M. Brueckmann, S.J. Pocock, F. Zannad, and M. Packer, for the EMPEROR-Preserved Trial Investigators*

EMPEROR-**Perserved** 27%↓



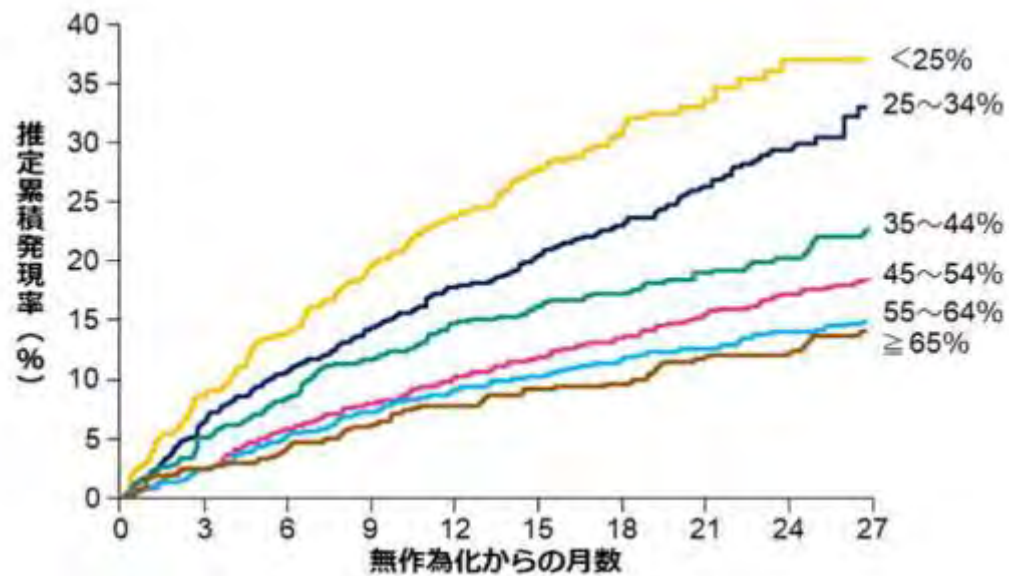
No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36
Placebo	2991	2945	2901	2855	2816	2618	2258	1998	1695	1414	1061	747	448
Empagliflozin	2997	2962	2913	2869	2817	2604	2247	1977	1684	1429	1081	765	446



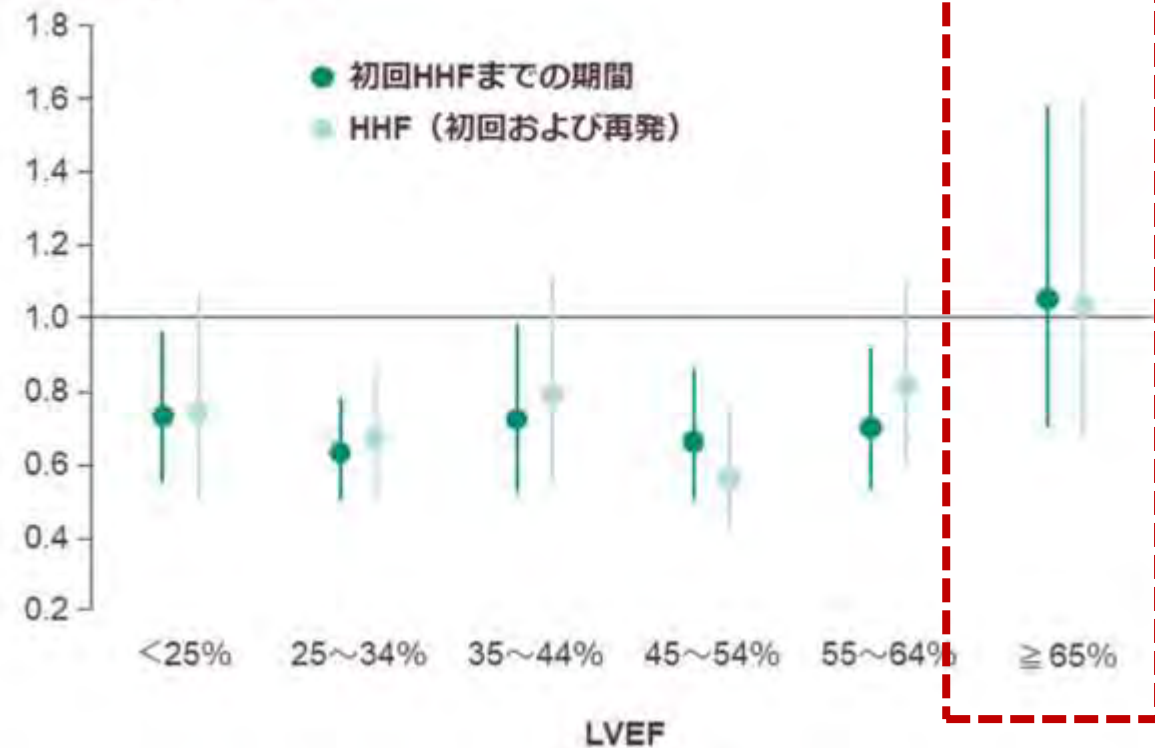
EMPEROR-Reduced/EMPEROR-Perservedプール解析 心血管死または心不全による入院の推定累積発生率

Eur Heart J 2022;43:416-26.

Placebo群における腎機能別 HHF（初回及び再発）累積発生曲線



ハザード比
(ジヤディアンス10mg : プラセボ)



Cardiovascular Outcomes in Patients Initiating First-Line Treatment of Type 2 Diabetes With Sodium-Glucose Cotransporter-2 Inhibitors Versus Metformin

A Cohort Study

HoJin Shin, BPharm, PhD; Sebastian Schneeweiss, MD, ScD; Robert J. Glynn, ScD, PhD; and Elisabetta Paterno, MD, DrPH

メトホルミンとの比較
心不全再入院は有意に減
性器感染症に注意

Safety and effectiveness of empagliflozin in Japanese patients with type 2 diabetes: final results of a 3-year post-marketing surveillance study

Kenji Kaku, Genroku Yamamoto, Yumiko Fukutami, Hiroo Uchiyama, Atsuhiko Kase

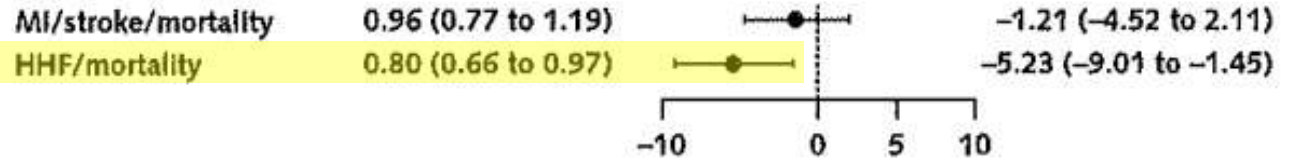
項目	頻度
尿路感染症	1.07 %
性器感染症	0.66 %
脱水	0.50 %
下肢切断	0.04 %

Table3より演者抜粋作成

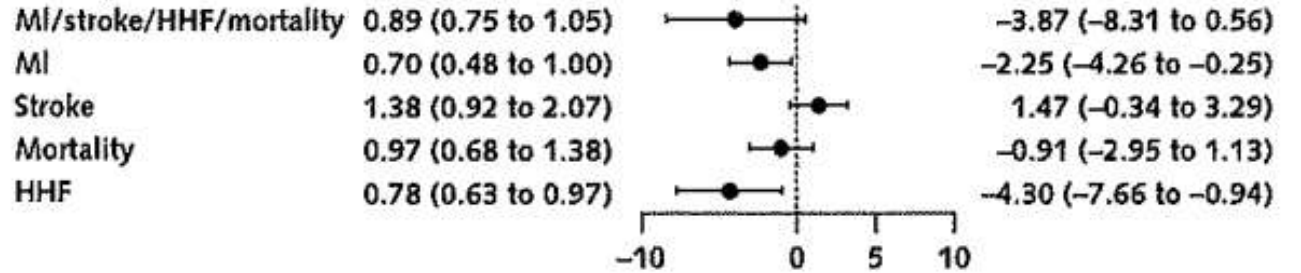
Outcomes

SGLT-2I Versus Metformin IRD per 1000 PYs (95% CI)

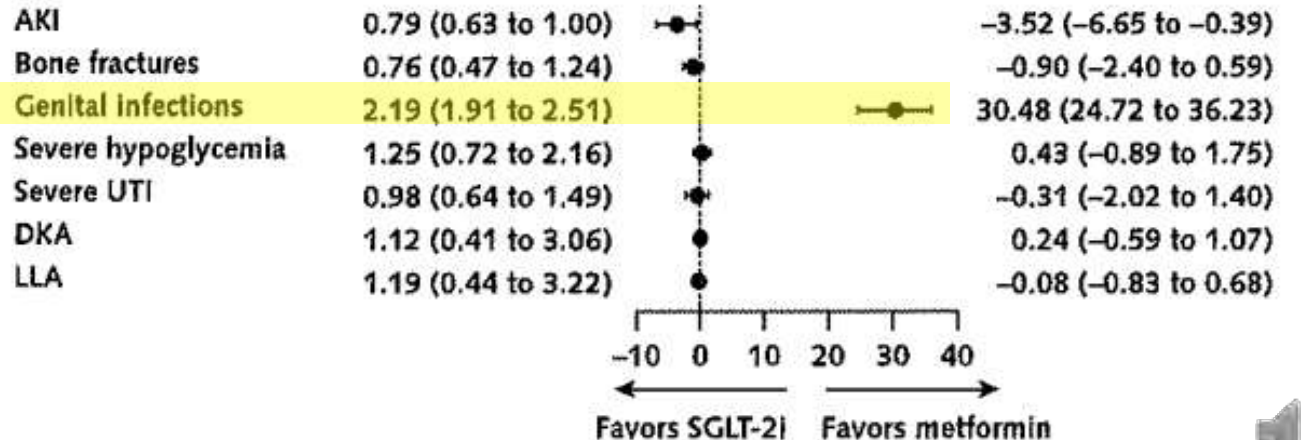
Primary



Secondary



Safety



Estimating lifetime benefits of comprehensive disease-modifying pharmacological therapies in patients with heart failure with reduced ejection fraction: a comparative analysis of three randomised controlled trials

Muthiah Vaduganathan¹, Brian Claggett¹, Pardeep Jhund², Jonathan W Cunningham³, João Pedro Ferreira^{1,4,5,6,7}, Faeze Zannad⁸, Milton Packer^{9,10}, Gregg Fonarow¹⁰, John McMurray², Scott Solomon¹¹

Lancet. 2020 Jul 11;396(10244):121-128.

20年間で治療進歩

ARNI, β遮断薬, MRA, SGLT2阻害薬併用の生存延長効果

基本処方

追加

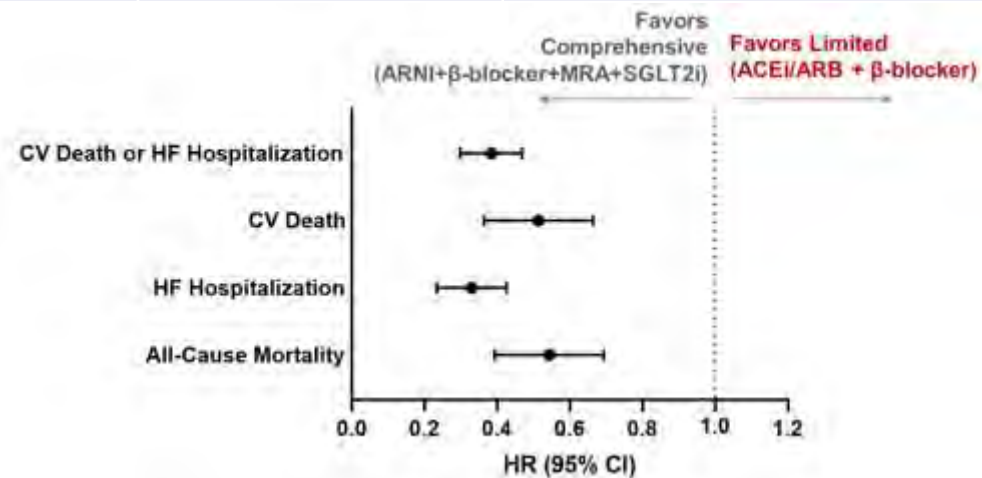
さらに追加

	心血管死	心不全入院	心血管死 + 心不全入院	全死亡
EMPHASIS-HF	0.76	0.58	0.63	0.76
PARADIGM-HF ARNI	0.82	0.70	0.74	0.83
DAPA-HF SGLT2i	0.80	0.79	0.80	0.84
3つをかけたもの	0.50	0.32	0.37	0.53

20年間での薬物治療で

入院は **1/3**

死亡は **1/2** に減?



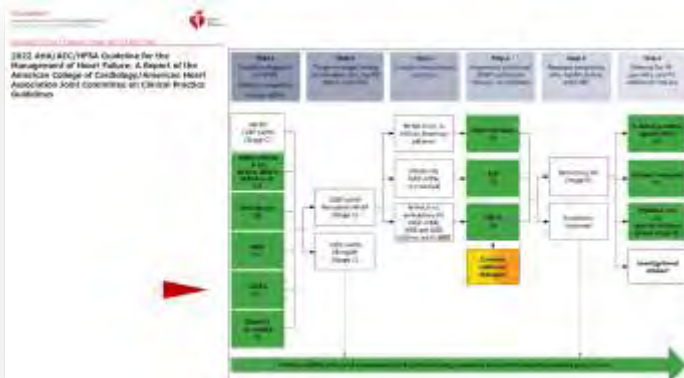
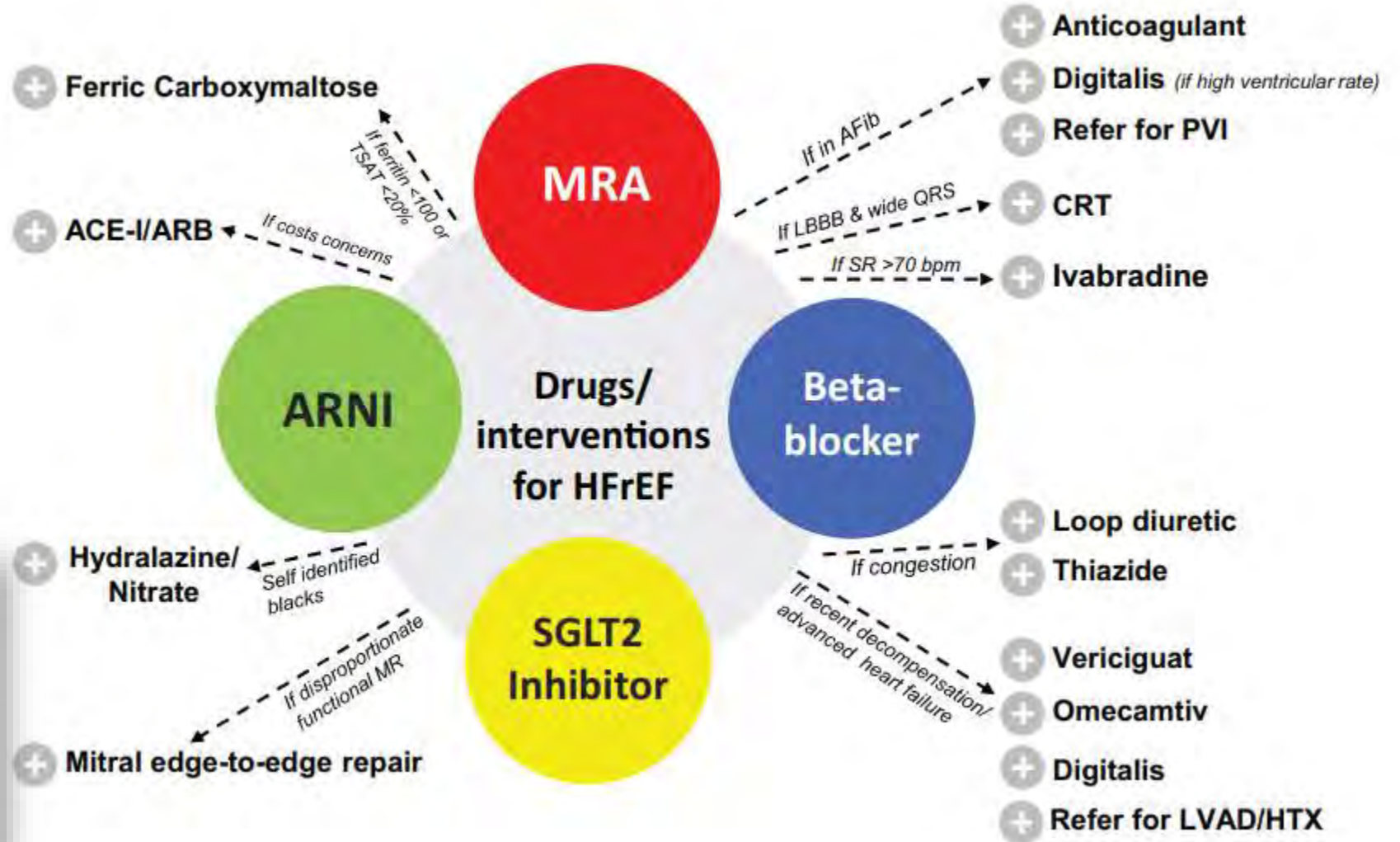
SGLT2阻害薬はClass I

Heart failure drug treatment: the fantastic four

Johann Bauersachs *

Department of Cardiology and Angiology, Hannover Medical School, Hannover, Germany

Online publication ahead of print 11 January 2021



Gliflozins in the Management of Cardiovascular Disease

Eugene Braunwald, M.D.

May 26, 2022

N Engl J Med 2022; 386:2024-2034

DOI: 10.1056/NEJMra2115011

「変わる」
糖尿病薬→心腎治療薬

- 1) Phlorizinはリンゴ樹皮抽出物、尿細管でSGLT2阻害→ブドウ糖再吸収阻害→尿糖排出
- 2) 経口SGLT2阻害薬は田辺製薬が開発、RCTで心血管リスク確認→心腎保護確認
- 3) **EMPA-REG2015で心血管疾患14%減、2-3週で効果発現、心不全入院35%減**
- 4) **SGLT2阻害薬で心血管イベント減少、心不全入院はすべての試験で減少**
- 5) **SGLT2阻害薬の心腎保護効果は血糖と無関係、HFpEFにも効果あり (EF25-65%)**
- 6) SGLT2阻害薬は腎機能無関係に透析、腎移植、腎死減 (RR0.67)、初期GFR dipあり
- 7) SGLT2阻害→尿細管Na↑→緻密班が輸入細動脈縮小→過剰ろ過↓→腎改善
- 8) 心臓への作用機序不明、ミトコンドリア機能改善？心筋Na濃度減？炎症軽減？異所性脂肪減？
- 9) 副作用：陰部、尿路感染症、血糖正常ケトアシドーシス、足趾切断？
- 10) SGLT2阻害薬で心房細動/粗動2割減、心室性不整脈、突然死3割減
- 11) SGLT2阻害薬とGLP-1受容体作動薬併用は相乗効果あり



RESEARCH

Open Access



Comparison of cardiovascular outcomes between SGLT2 inhibitors in diabetes mellitus

Yuta Suzuki^{1,2*}, Hidehiro Kaneko^{1,3*}, Akira Okada⁴, Hidetaka Itoh¹, Satoshi Matsuoka¹, Katsuhito Fujii^{1,3}, Nobuaki Michihata⁵, Taisuke Jo⁵, Norifumi Takeda¹, Hiroyuki Morita¹, Kentaro Kamlya², Atsuhiko Matsunaga², Junya Ako⁶, Koichi Node⁷, Hideo Yasunaga⁸ and Issei Komuro¹

基本的にはClass Effect

心不全

心筋梗塞

狭心症

脳梗塞

心房細動

	Number	Events	Incidence	Model 1	Model 2	Model 3	Hazard Ratio (95% Confidence Interval)	P value
Heart Failure								
Empagliflozin	5,302	155	156.7 (133.9-183.5)	1 [Reference]	1 [Reference]	1 [Reference]		0.1415
Dapagliflozin	4,681	171	159.7 (137.5-185.5)	0.98 (0.79-1.23)	0.99 (0.80-1.23)	1.02 (0.81-1.27)		
Canagliflozin	4,411	160	168.7 (144.5-197.0)	1.06 (0.85-1.32)	1.06 (0.85-1.32)	1.08 (0.87-1.35)		
Other SGLT2-Inhibitors	10,921	369	140.0 (126.5-155.1)	0.86 (0.71-1.04)	0.86 (0.71-1.04)	0.88 (0.73-1.07)		
Myocardial Infarction								
Empagliflozin	5,302	27	26.8 (18.4-39.1)	1 [Reference]	1 [Reference]	1 [Reference]		0.4569
Dapagliflozin	4,681	27	24.7 (17.0-36.1)	0.87 (0.51-1.49)	0.88 (0.51-1.51)	0.77 (0.45-1.33)		
Canagliflozin	4,411	26	26.9 (18.3-39.5)	0.98 (0.57-1.68)	0.97 (0.57-1.67)	0.88 (0.51-1.52)		
Other SGLT2-Inhibitors	10,921	63	23.5 (18.3-30.0)	0.81 (0.51-1.28)	0.81 (0.52-1.29)	0.70 (0.43-1.11)		
Angina Pectoris								
Empagliflozin	5,302	137	138.4 (117.1-163.6)	1 [Reference]	1 [Reference]	1 [Reference]		0.8367
Dapagliflozin	4,681	162	151.9 (130.2-177.1)	1.10 (0.87-1.38)	1.11 (0.88-1.39)	1.03 (0.82-1.30)		
Canagliflozin	4,411	140	147.4 (124.9-174.0)	1.07 (0.84-1.35)	1.07 (0.84-1.35)	1.03 (0.81-1.31)		
Other SGLT2-Inhibitors	10,921	376	143.6 (129.8-158.9)	1.04 (0.86-1.27)	1.04 (0.86-1.27)	0.96 (0.79-1.17)		
Stroke								
Empagliflozin	5,302	57	56.9 (43.9-73.8)	1 [Reference]	1 [Reference]	1 [Reference]		0.8607
Dapagliflozin	4,681	70	64.5 (51.0-81.5)	1.13 (0.80-1.61)	1.16 (0.82-1.64)	1.10 (0.77-1.56)		
Canagliflozin	4,411	54	56.0 (42.9-73.1)	0.98 (0.68-1.43)	0.99 (0.68-1.43)	0.96 (0.66-1.40)		
Other SGLT2-Inhibitors	10,921	159	59.5 (51.0-69.5)	1.04 (0.77-1.41)	1.05 (0.77-1.42)	0.98 (0.72-1.33)		
Atrial Fibrillation								
Empagliflozin	5,302	30	29.8 (20.9-42.7)	1 [Reference]	1 [Reference]	1 [Reference]		0.2561
Dapagliflozin	4,681	22	20.1 (13.2-30.5)	0.65 (0.37-1.13)	0.66 (0.38-1.14)	0.63 (0.36-1.09)		
Canagliflozin	4,411	27	27.9 (19.1-40.7)	0.92 (0.55-1.54)	0.92 (0.54-1.54)	0.90 (0.54-1.53)		
Other SGLT2-Inhibitors	10,921	60	22.3 (17.3-28.8)	0.72 (0.46-1.12)	0.73 (0.47-1.13)	0.70 (0.44-1.09)		



日本人でも効く

全体

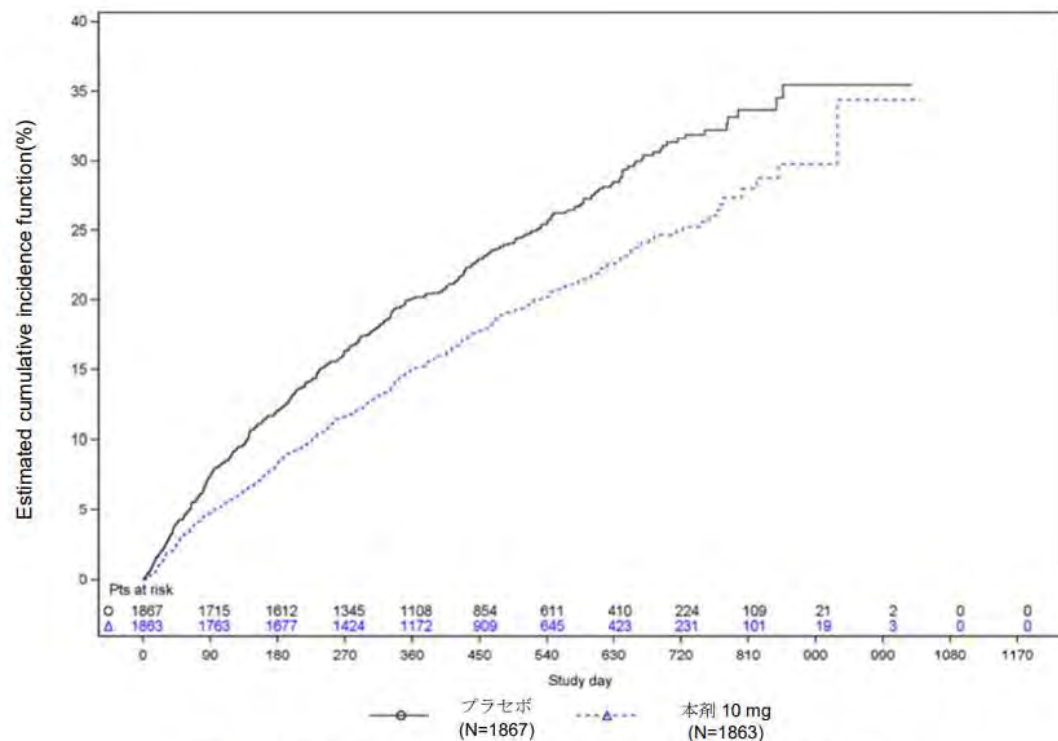


図1 心血管死又は心不全による入院（初回）までの期間
（推定累積発現関数（非心血管死を競合リスクとして考慮）：Randomized set（全体集団））

日本人

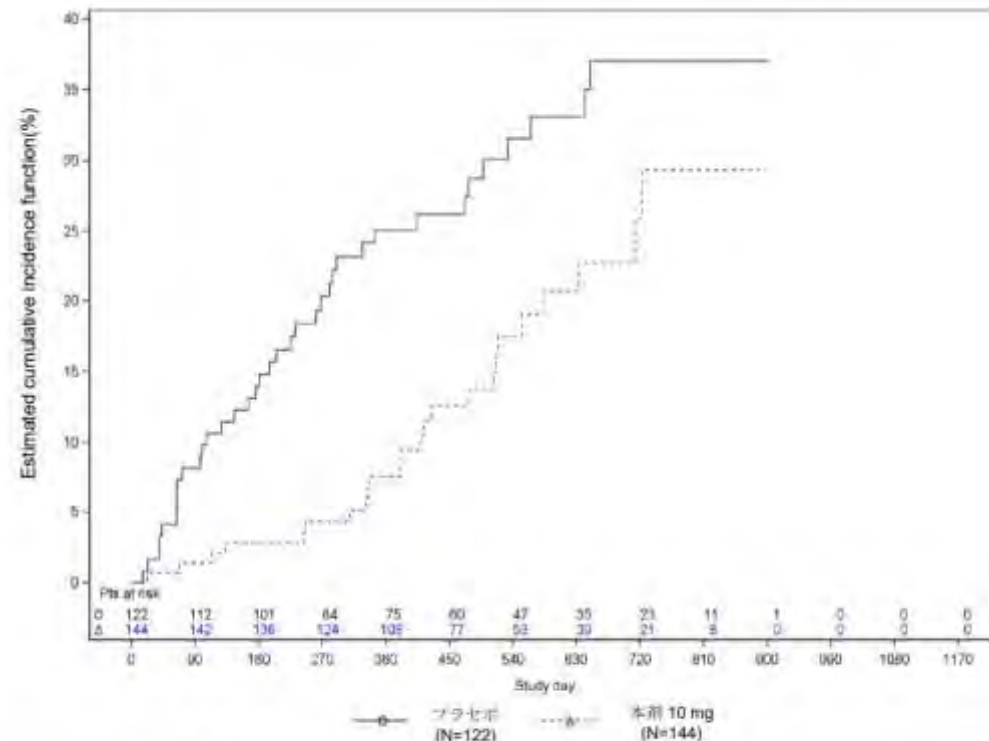


図2 心血管死又は心不全による入院（初回）までの期間
（推定累積発現関数（非心血管死を競合リスクとして考慮）：Randomized set（日本人集団））



Uric acid and sodium-glucose cotransporter-2 inhibition with empagliflozin in heart failure with reduced ejection fraction: the EMPEROR-reduced trial

Wolfram Doehner^{1,2}, Stefan D. Anker³, Javed Butler^{4,5}, Faleh Zannad⁶, Gerasimos Filippatos⁷, João Pedro Ferreira^{8,9}, Afshin Salsali^{7,8}, Carolyn Kammerer^{10,11}, Martina Brueckmann^{10,11}, Stuart J. Pocock¹², James L. Januzzi¹³, and Milton Packer¹⁴

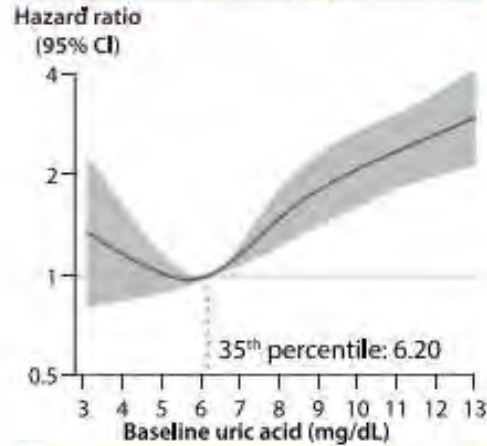
結論

高尿酸血症はHFで一般的、進行した疾患の重症度および死亡率の増加の独立した予測因子。

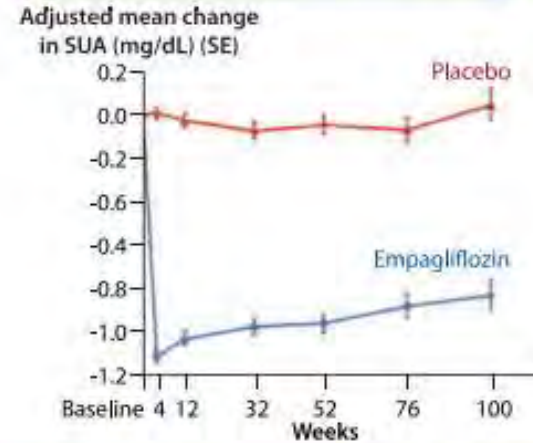
エンパグリフロジンは、SUAレベルおよび高尿酸血症に関連する臨床事象の迅速かつ持続的な低下を誘導。

主要転帰に対するエンパグリフロジンの利点は、SUAとは無関係に観察

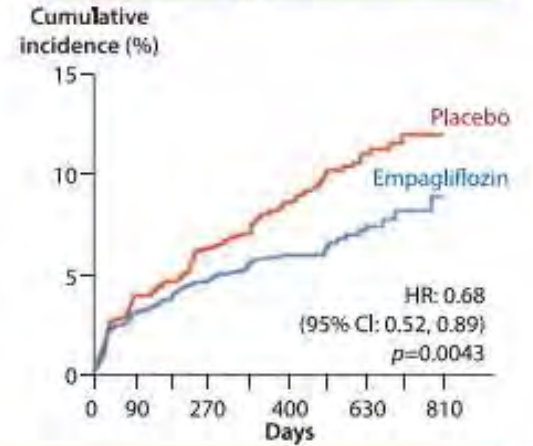
Relationship between baseline SUA and primary endpoint*



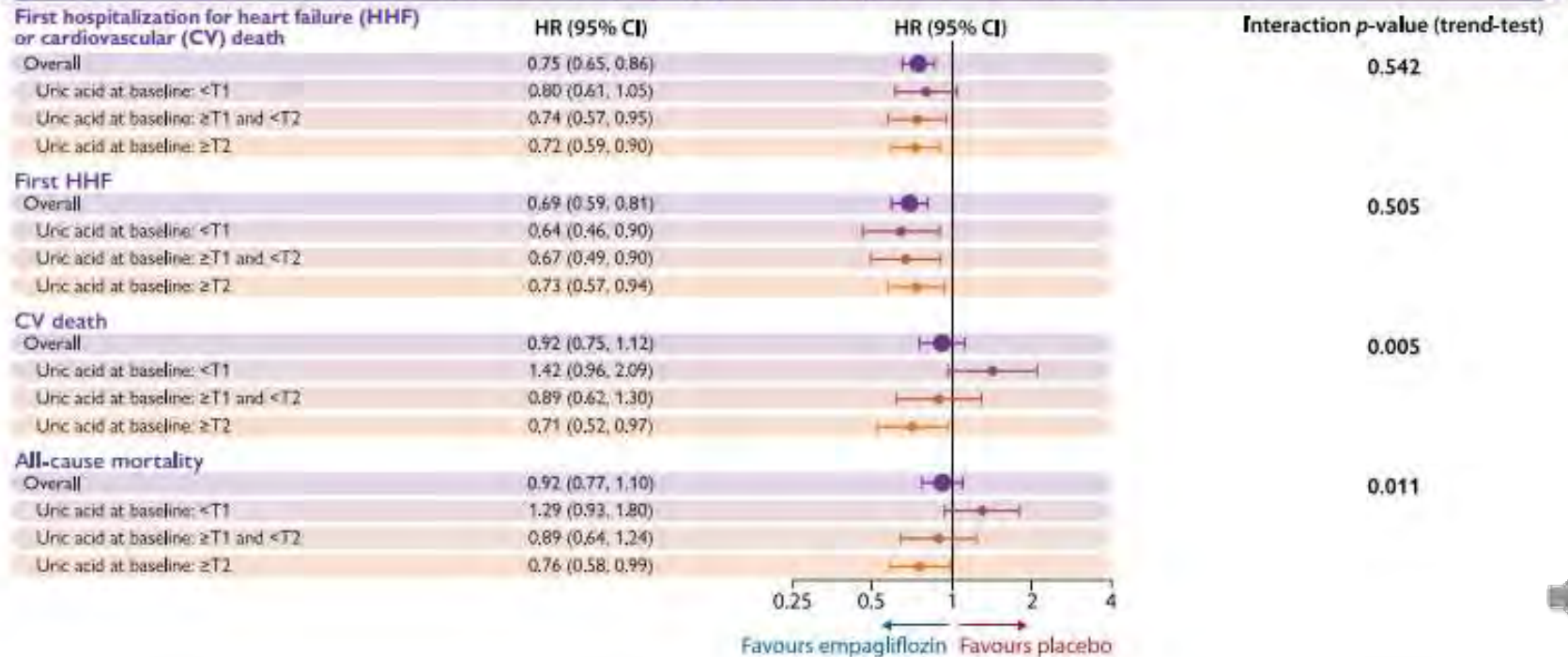
Treatment effect on SUA levels



Cumulative incidence of clinically relevant hyperuricaemia†



Treatment effect on major outcomes by tertile SUA at baseline†

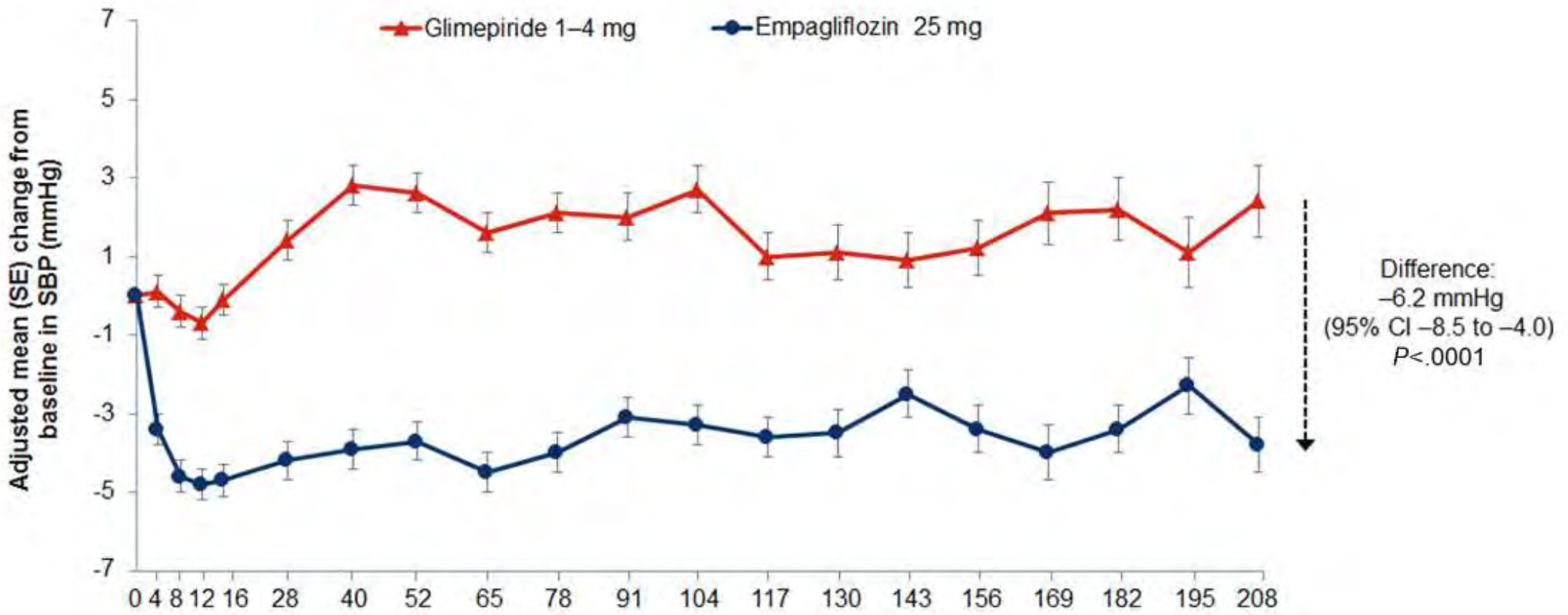


Empagliflozin compared with glimepiride in metformin-treated patients with type 2 diabetes: 208-week data from a masked randomized controlled trial

Martin Ridderstråle MD¹ | Julio Rosenstock MD² | Knut R. Andersen BSc³ | Hans J. Woerle MD⁴ | Afshin Salsali MD⁵ | on behalf of the EMPA-REG H2H-SU trial investigators
Diabetes Obes Metab. 2018;20:2768–2777.

Glimepirideと比較して SGLT2阻害薬は血圧を下げる

(B)



Effects of empagliflozin on blood pressure and markers of arterial stiffness and vascular resistance in patients with type 2 diabetes

R. Chilton¹, I. Tikkanen², C. P. Cannon³, S. Crowe⁴, H. J. Woerle⁴, U. C. Broedl⁴ & O. E. Johansen⁵

¹ Department of Medicine, University of Texas Health Science Center, San Antonio, TX, USA

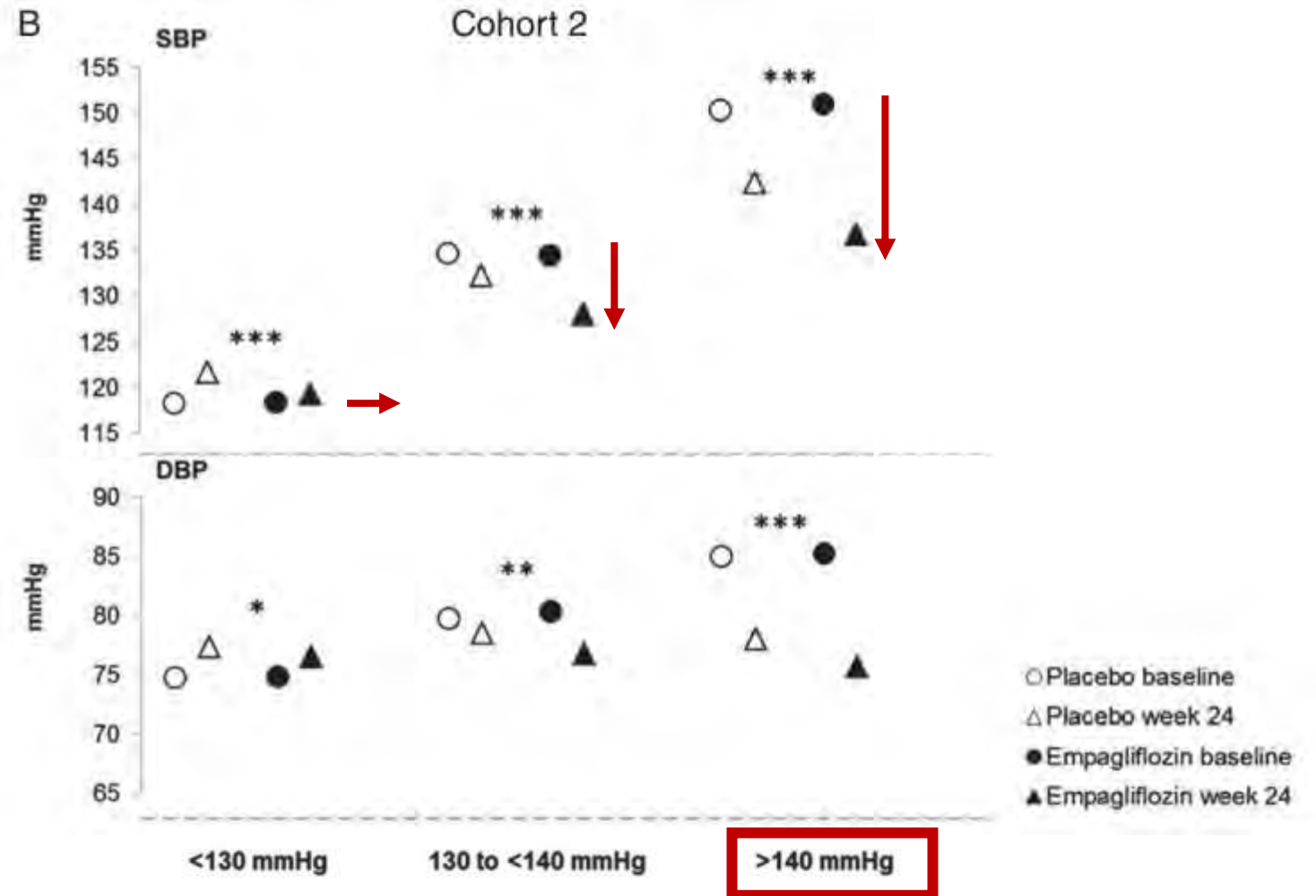
² Helsinki University Hospital and Minerva Institute for Medical Research, University of Helsinki, Helsinki, Finland

³ Department of Cardiology, Harvard Clinical Research Institute, Boston, MA, USA

⁴ Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany

⁵ Boehringer Ingelheim Norway KS, Asker, Norway

血圧が高いほど
収縮期血圧低下

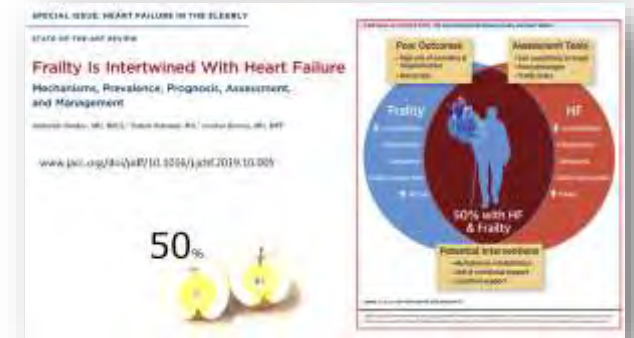


Efficacy and Safety of Dapagliflozin According to Frailty in Heart Failure With Reduced Ejection Fraction

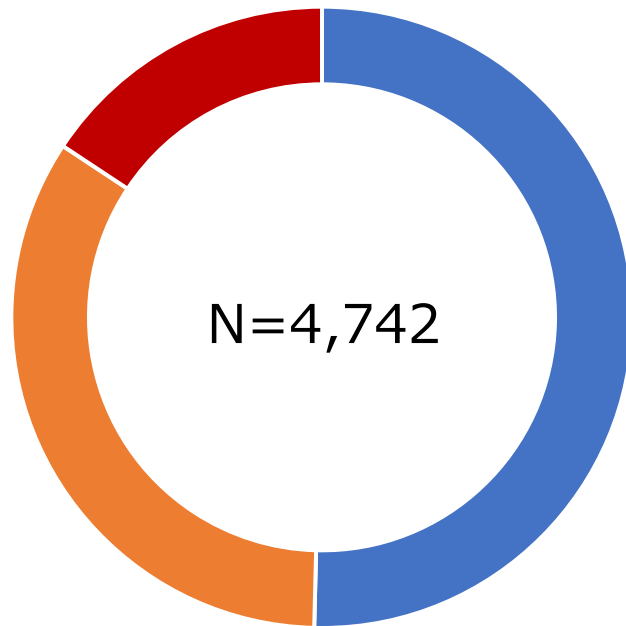
A Post Hoc Analysis of the DAPA-HF Trial

Jawed H. Butt, MD; Pooja Dewan, MB, ChB; Bela Merkely, MD, PhD; Jan Belohlávek, MD, PhD; Jaroslaw Drozd, MD, PhD; Masafumi Kitakaze, MD, PhD; Silvio E. Inzucchi, MD; Mikhail N. Kosiborod, MD; Felipe A. Martinez, MD; Sergey Tereshchenko, MD, PhD; Piotr Ponikowski, MD, PhD; Olof Bengtsson, Ph Lic; Daniel Lindholm, MD, PhD; Anna Maria Langkilde, MD, PhD; Morten Schou, MD, PhD; Mikaela Sjöstrand, MD, PhD; Scott D. Solomon, MD; Marc S. Sabatine, MD, MPH; Chen-En Chiang, MD, PhD; Kieran F. Docherty, MBChB; Pardeep S. Jhund, MBChB, MSc, PhD; Lars Køber, MD, DMSc; and John J.V. McMurray, MD

Ann Intern Med. 2022 Apr 26. doi: 10.7326/M21-4776. Online ahead of print.

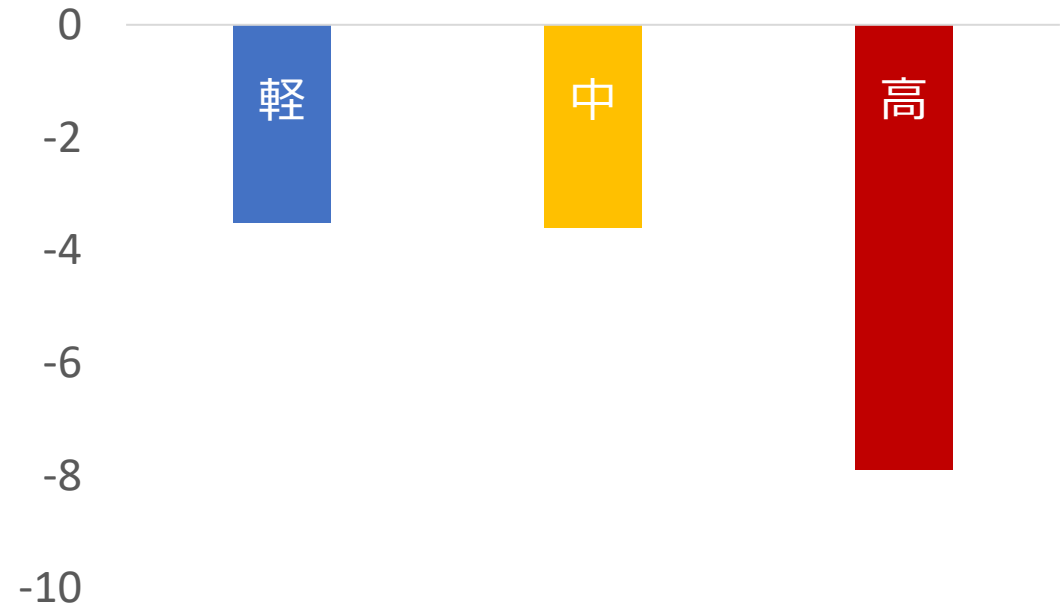


フレイル心不全患者に対してもDapagliplozinは有効



■ 軽度 ■ 中等度 ■ 高度

プラセボとの事象発生率



Efficacy and Safety of Dapagliflozin According to Frailty in Heart Failure With Reduced Ejection Fraction

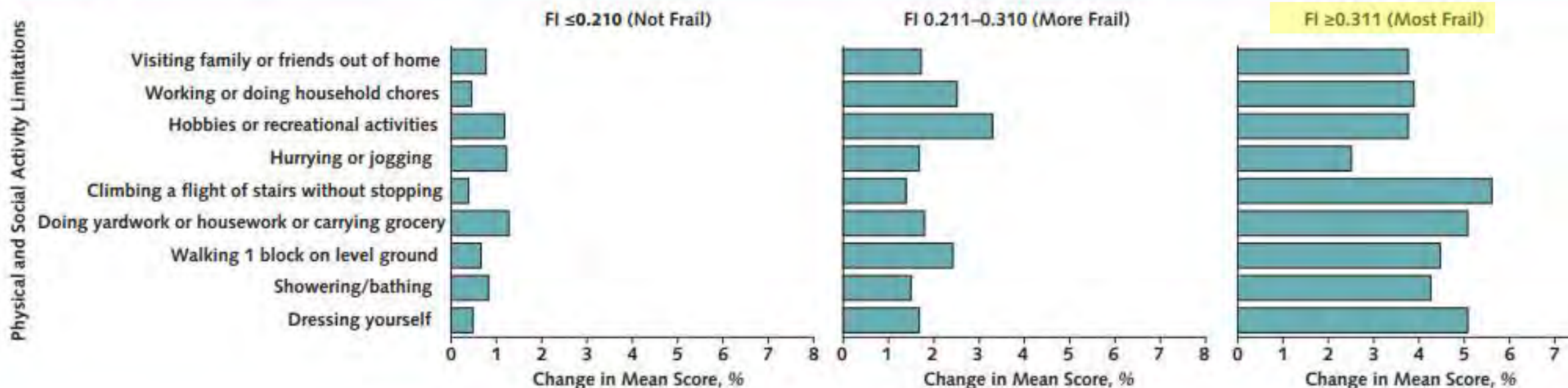
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高度フレイルが改善大

Ann Intern Med. 2022 Apr 26. doi: 10.7326/M21-4776. Online ahead of print.

Figure 2. Mean change in individual physical and social activity items from baseline to 8 months with dapagliflozin versus placebo according to FI.



Responses to the questions were scaled to 0 to 100, with higher score indicating a lesser degree of limitation. Responses of "limited for other reasons" or "did not do the activity" were not allocated a score. The question about "Intimate relationships with loved ones" was excluded as only 64% of patients with baseline data from the Kansas City Cardiomyopathy Questionnaire responded to this question. Higher FI indicates greater frailty. FI = Frailty Index.

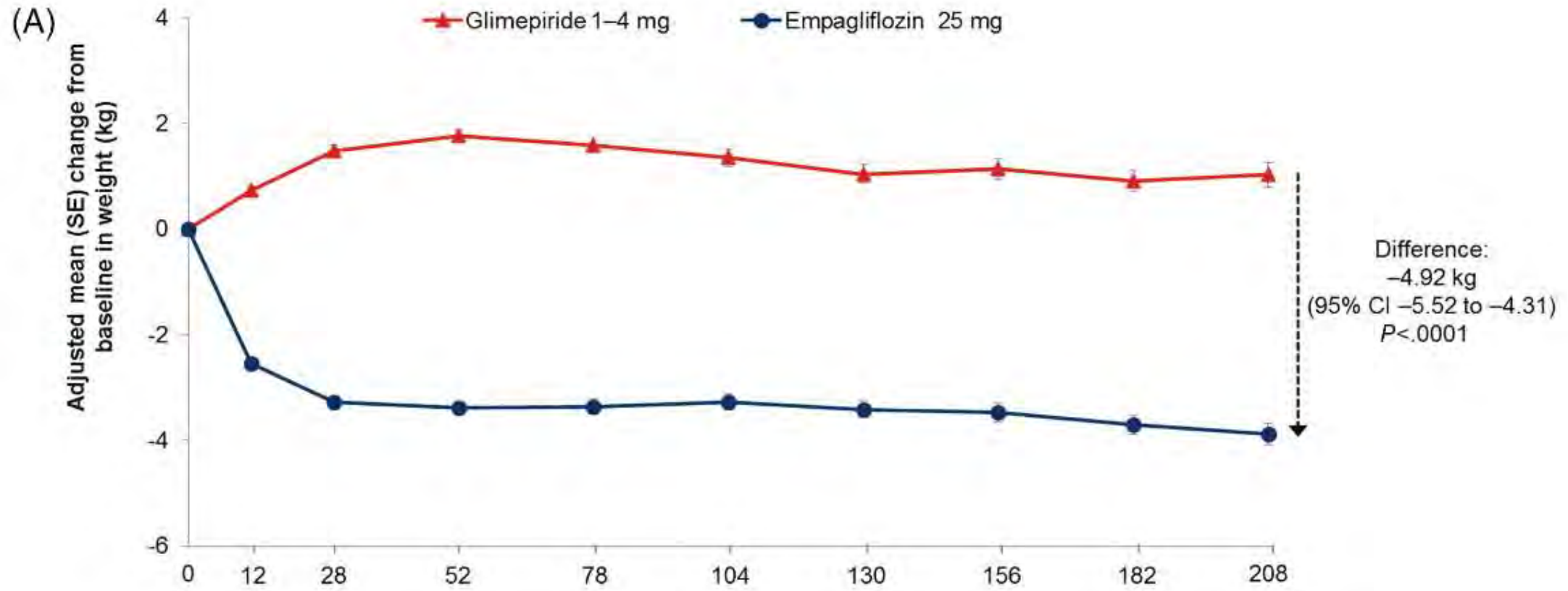
筋肉も減らないの？



Empagliflozin compared with glimepiride in metformin-treated patients with type 2 diabetes: 208-week data from a masked randomized controlled trial

Martin Ridderstråle MD¹ | Julio Rosenstock MD² | Knut R. Andersen BSc³ | Hans J. Woerle MD⁴ | Afshin Salsali MD⁵ | on behalf of the EMPA-REG H2H-SU trial investigators
Diabetes Obes Metab. 2018;20:2768–2777.

Glimepirideと比較して SGLT 2 阻害薬では**体重減**



Empagliflozin compared with glimepiride in metformin-treated patients with type 2 diabetes: 208-week data from a masked randomized controlled trial

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Hans J. Woerle MD⁴ | Afshin Salsali MD⁵ | on behalf of the EMPA-REG H2H-SU trial
investigators
Diabetes Obes Metab. 2018;20:2768-2777.

Supplement Table4より演者作図

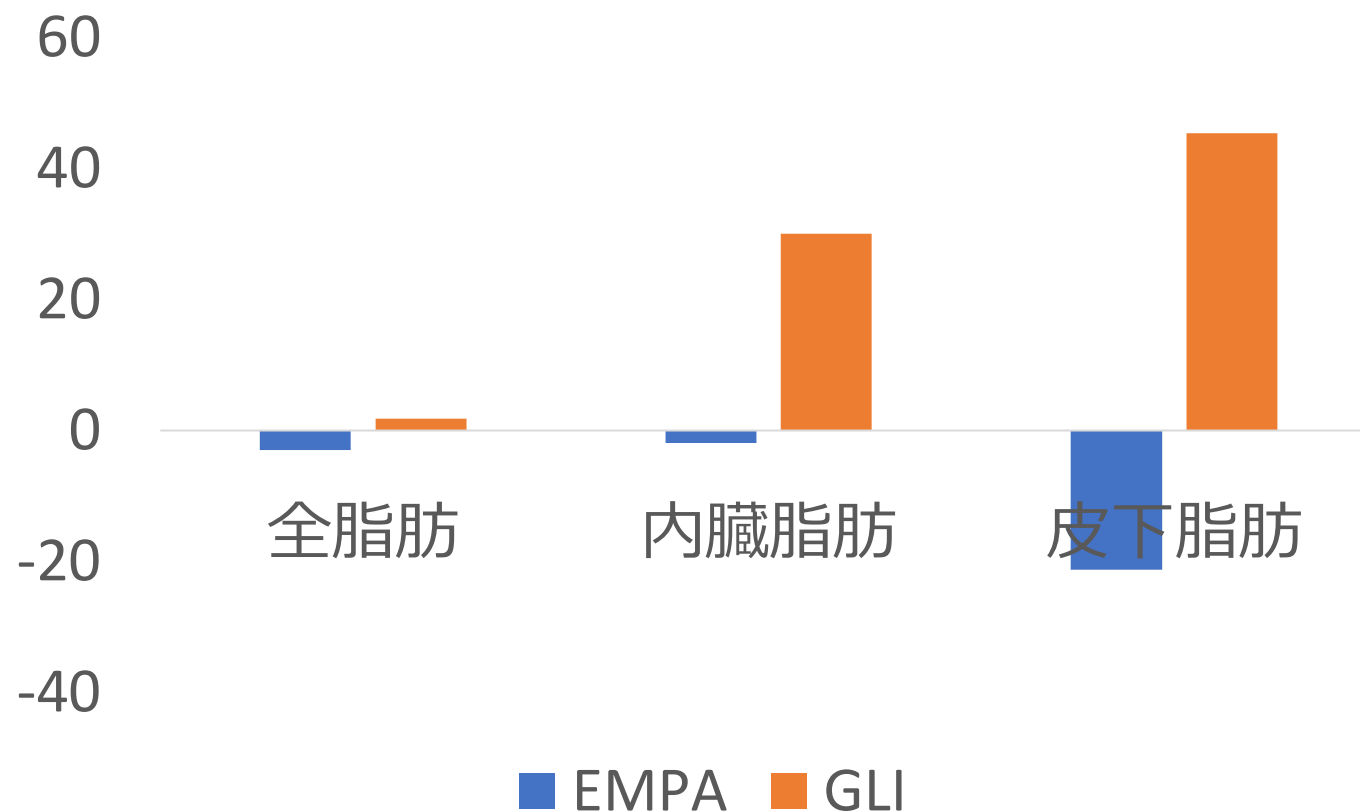
除脂肪体重

EMPA -0.01kg

GLI 0.27kg

Glimepirideと比較して SGLT2阻害薬では**脂肪減**

脂肪量の208週後変化



全脂肪はkg、内臓脂肪、皮下脂肪はcm²



BRIEF COMMUNICATION

OPEN

Check for updates

Dapagliflozin increases the lean-to total mass ratio in type 2 diabetes mellitus

Vaneza Lira W. Wolf¹, Ikaro Breder¹, Luiz Sérgio F. de Carvalho^{1,2}, Alexandre A. S. Soares³, Riobaldo M. Cintra¹, Joaquim Barreto¹, Daniel B. Munhoz¹, Sheila T. Kimura-Medorima¹, Wilson Nadruz³, Gil Guerra-Júnior⁴, Thiago Quinaglia¹, Elza Muscelli¹, Andrei C. Sposito^{1,5*} on behalf of Addenda-BHS2 trial investigators

Nutrition & Diabetes (2021)11:17; <https://doi.org/10.1038/s41387-021-00160-5>

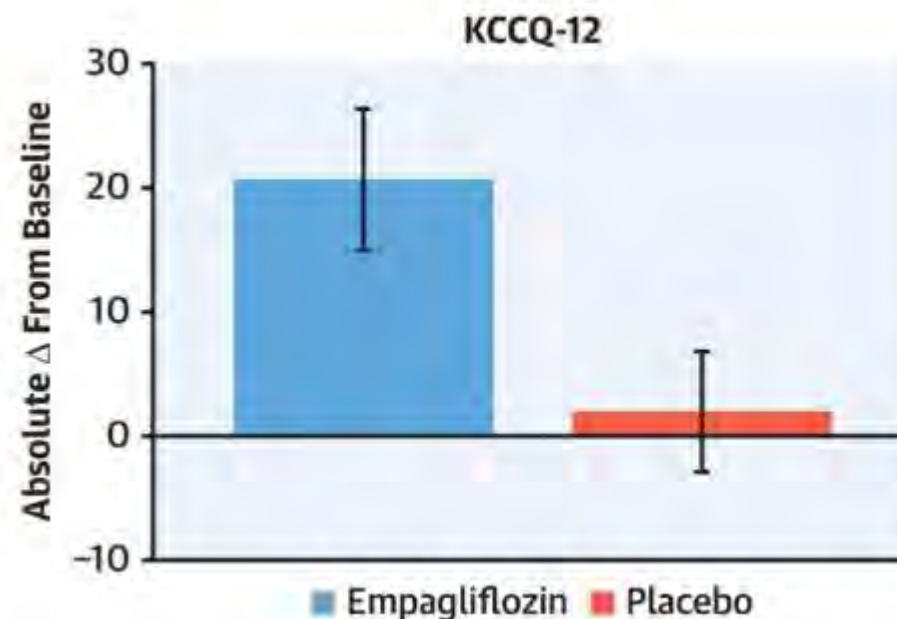
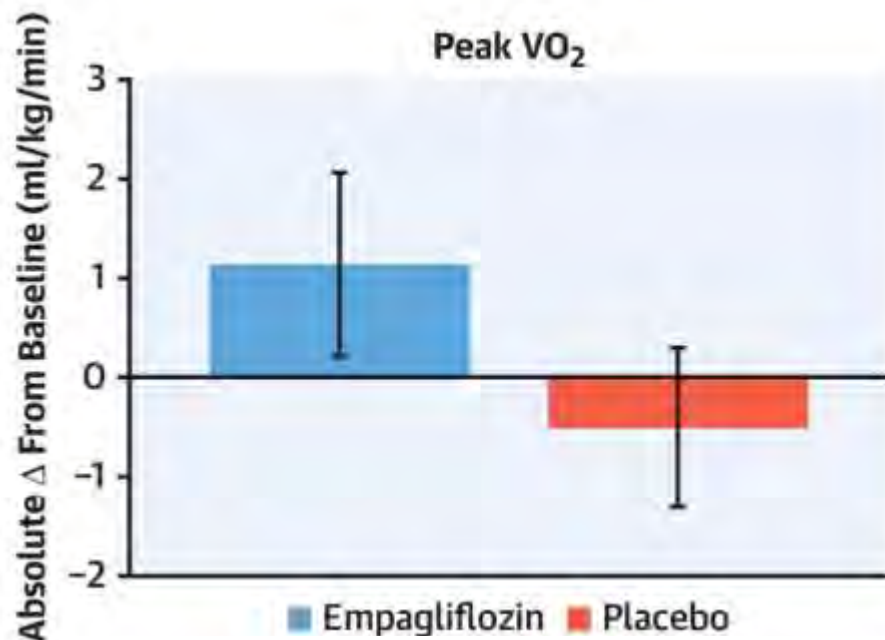
Table 2. Changes in primary and secondary outcomes.

	Dapagliflozin N 44	Glibenclamide N 45	95% CI of the difference	p-value
BMI (kg/m ²)	−1.0 (−1.2 to 0.7)	0.4 (0.1 to 0.7)	−1.39 (−1.76 to −1.01)	<0.001
Lean mass/total mass ratio	0.012 (0.00 to 0.15)	0.001 (−0.00 to 0.00)	0.011 (0.006 to 0.015)	<0.001
Total lean mass (g)	−347 (−761 to −106)	929 (575 to 1283)	−0.41 (−0.60 to −0.23)	<0.001
Peripheral lean mass (g)	−391 (−615 to −166)	450 (188 to 711)	−840 (−1181 to −500)	<0.001
Total Fat mass (g)	−1959 (−2307 to −1429)	413 (76 to 749)	−2372 (−2916 to −1827)	<0.001
Total body mass (g)	−2741 (−3360–1945)	1060 (140–1836)	−3535 (−4339 to −2732)	<0.001

Glibenclamideに比べてDapagliflozin投与により
体重に占める**Lean mass**の割合が1.2%**上昇**する



運動耐容能とQOLは改善する



CPET

Peak VO ₂ , ml/min/kg	15.3 ± 4.3	16.4 ± 4.4	1.1 ± 2.6	14.5 ± 3.9	14.0 ± 4.2	-0.5 ± 1.9	0.017
VE/VCO ₂	29.5 ± 4.6	28.6 ± 4.8	-1.2 ± 3.4	27.4 ± 5.4	28.0 ± 6.7	0.5 ± 3.9	0.09
OUES	1,522 ± 425	1,633 ± 510	111 ± 267	1,630 ± 506	1,485 ± 570	-145 ± 318	<0.001
6-min walk, m	420 ± 93.4	501 ± 100	81 ± 64	452 ± 101	417 ± 113	-35 ± 68	<0.001
KCCQ-12		88.3 ± 13.3	21 ± 18	71.8 ± 22	73.6 ± 23.3	1.9 ± 15	<0.001



Review
Could SGLT2 Inhibitors Improve Exercise Intolerance in Chronic Heart Failure?

Suzanne N. Voorrips *¹, Huitzilihuitl Saucedo-Orozco², Pablo I. Sánchez-Aguilera, Rudolf A. De Boer,
Int. J. Mol. Sci. **2022**, *23*, 8631. <https://doi.org/10.3390/ijms23158631>

A 心臓

収縮能 ↑、拡張能 ↑
心筋リモデリング ↓

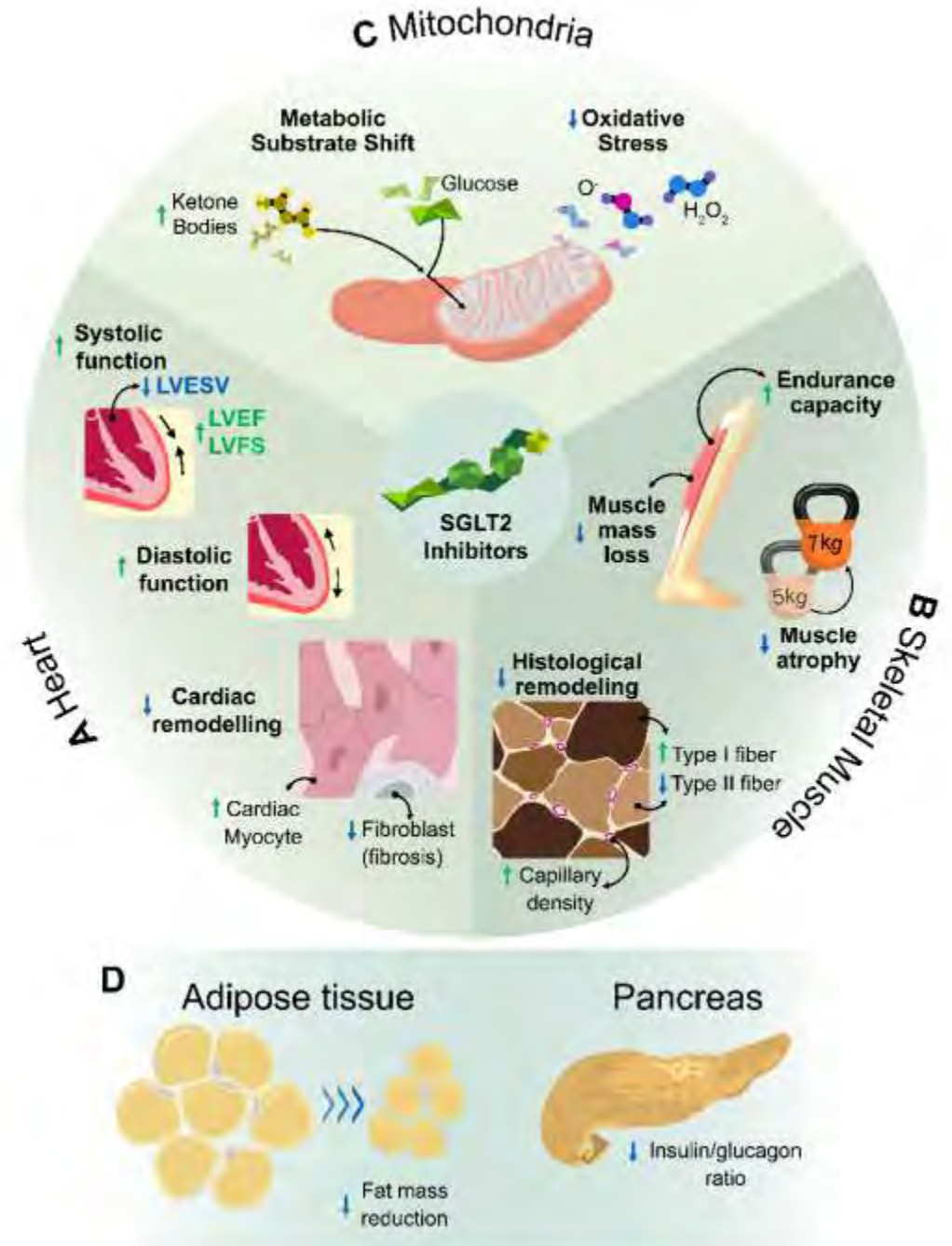
B 骨格筋

筋萎縮 ↓
筋量喪失 ↓
持久力 ↑
組織学的リモデリング ↓





C ミトコンドリア

代謝器質変化
酸化ストレス ↓

D 脂肪組織、膵臓



Safety and effectiveness of empagliflozin according to body mass index in Japanese patients with type 2 diabetes: a subgroup analysis of a 3-year post-marketing surveillance study

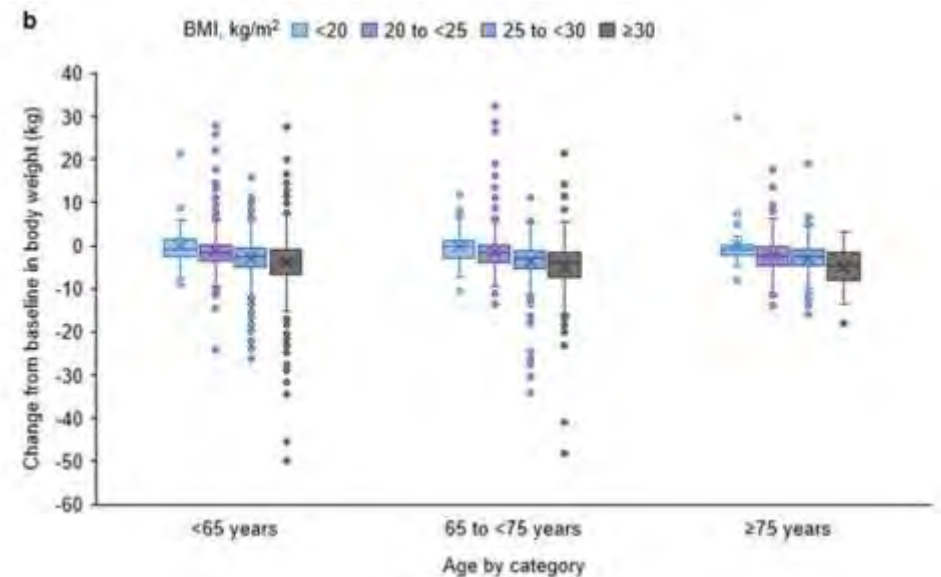
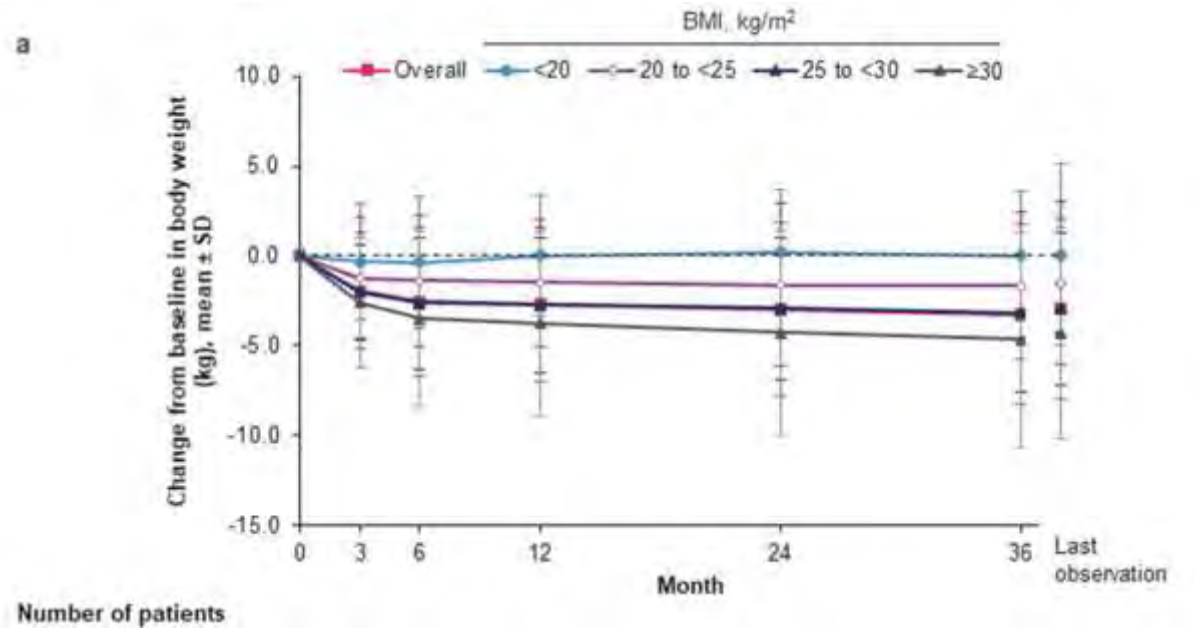
Kohei Kaku , Kazuhiro Yamamoto , Yumiko Fukushima, Seiko Mizuno & Daisuke Nitta  

Expert Opinion on Drug Safety

<https://doi.org/10.1080/14740338.2022.2062322>

過体重の例ほど体重減
BMI<20では減らず

高齢者でも過体重例で体重減





フレイル対象では筋ロスの心配より
開始時期の腎機能低下度が問題



Gliflozins in the Management of Cardiovascular Disease

Eugene Braunwald, M.D.

May 26, 2022

N Engl J Med 2022; 386:2024-2034

DOI: 10.1056/NEJMra2115011

「変わる」
糖尿病薬→心腎治療薬

- 1) Phlorizinはリンゴ樹皮抽出物、尿細管でSGLT2阻害→ブドウ糖再吸収阻害→尿糖排出
- 2) 経口SGLT2阻害薬は田辺製薬が開発、RCTで心血管リスク確認→心腎保護確認
- 3) EMPA-REG2015で心血管疾患14%減、2-3週で効果発現、心不全入院35%減
- 4) SGLT2阻害薬で心血管イベント減少、心不全入院はすべての試験で減少
- 5) SGLT2阻害薬の**心腎保護効果は血糖と無関係**、HFpEFにも効果あり (EF25-65%)
- 6) SGLT2阻害薬は腎機能無関係に透析、腎移植、腎死減 (RR0.67)、初期GFR dipあり
- 7) SGLT2阻害→尿細管Na↑→緻密班が輸入細動脈縮小→過剰ろ過↓→腎改善
- 8) 心臓への作用機序不明、ミトコンドリア機能改善？心筋Na濃度減？炎症軽減？異所性脂肪減？
- 9) 副作用：陰部、尿路感染症、血糖正常ケトアシドーシス、足趾切断？
- 10) **SGLT2阻害薬で心房細動/粗動2割減、心室性不整脈、突然死3割減**
- 11) SGLT2阻害薬とGLP-1受容体作動薬併用は相乗効果あり



ORIGINAL INVESTIGATION

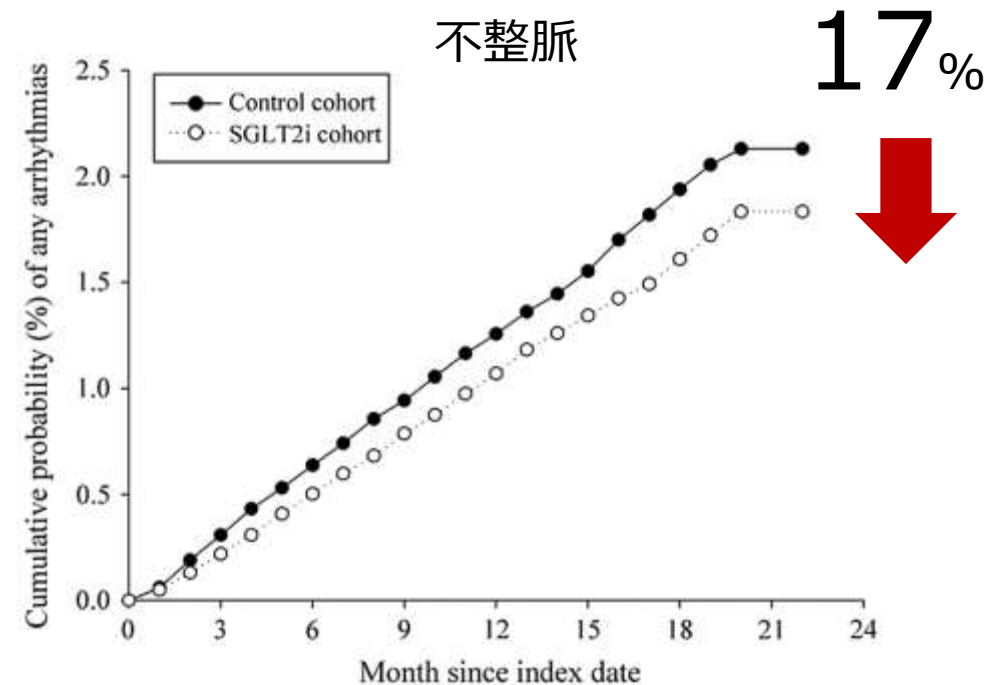
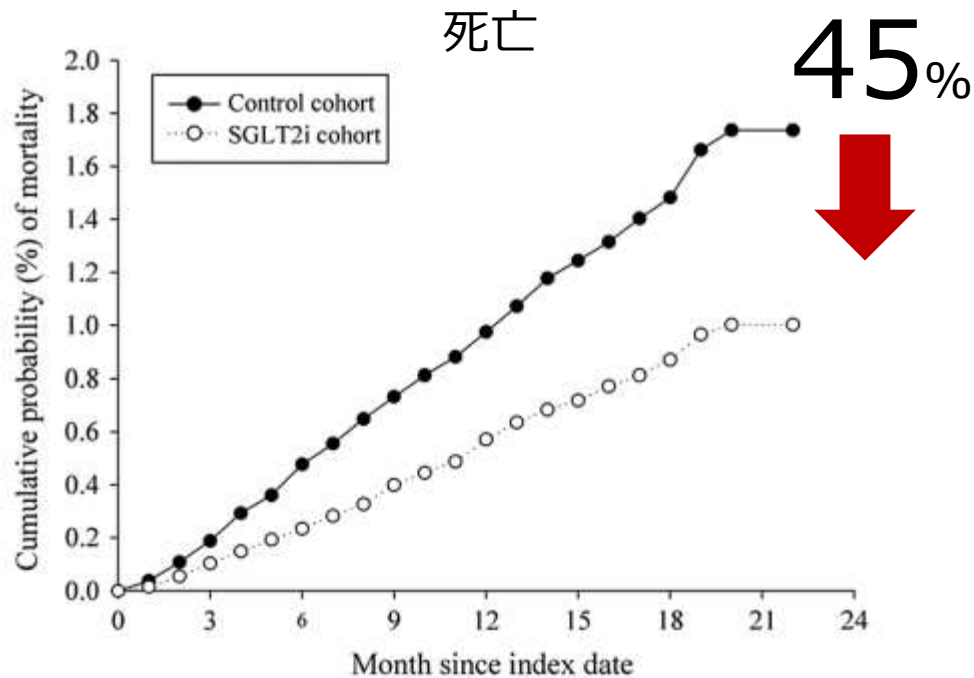
Open Access

The association between SGLT2 inhibitors and new-onset arrhythmias: a nationwide population-based longitudinal cohort study



Hung-Yi Chen¹, Jing-Yang Huang², Wun-Zhih Siao^{3†} and Gwo-Ping Jong^{3†*}

上室性不整脈も
心室性不整脈も
心房細動も減少



ORIGINAL INVESTIGATION

Open Access



The association between SGLT2 inhibitors and new-onset arrhythmias: a nationwide population-based longitudinal cohort study

年齢にかかわらず減少

Hung-Yi Chen¹, Jing-Yang Huang², Wun-Zhih Siao^{3†} and Gwo-Ping Jong^{3†*}

Table 3 Sensitivity analyses

Outcome	Non-SGLT2i			SGLT2i			Hazard Ratio (95% CI)	P value
	%	20 M KM (%)	Events/10,000 Ptms	%	20 KM (%)	Events/10,000 Ptms		
Age < 60 year and All-cause death	305 (0.60%)	0.60	6.42	147 (0.29%)	0.29	3.05	0.47 (0.35–0.63)	< 0.001
Age ≥ 60 year and All-cause death	361 (1.26%)	1.26	13.94	233 (0.81%)	0.81	8.93	0.57 (0.45–0.72)	< 0.001
Age < 60 year and NOA	452 (0.89%)	0.87	9.58	369 (0.73%)	0.72	7.70	0.81 (0.67–0.99)	0.042
Age ≥ 60 year and NOA	406 (1.42%)	1.40	15.82	352 (1.23%)	1.21	13.60	0.83 (0.68–1.01)	0.061

NOA new-onset arrhythmias, 10,000 Ptms per 10,000 patient months, SGLT2i sodium–glucose cotransporter 2 inhibitors

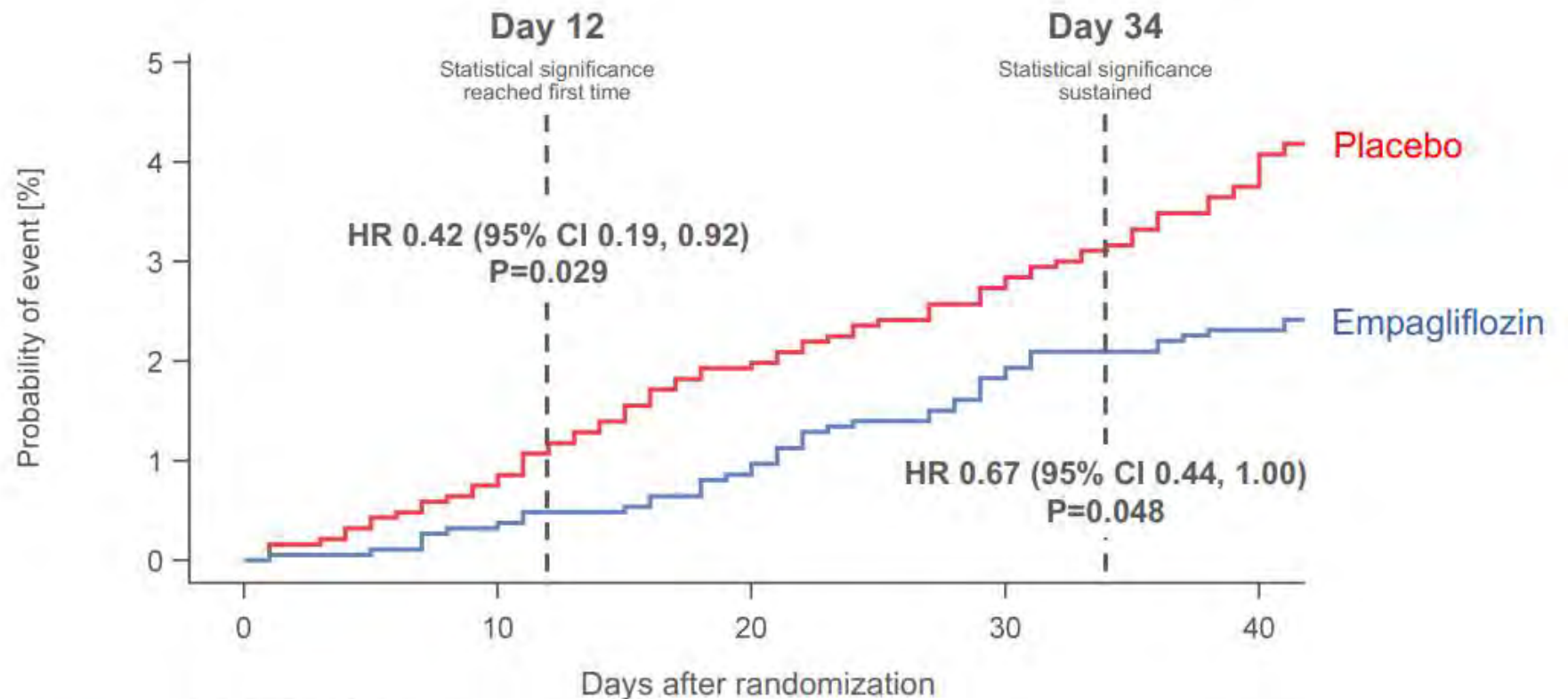


Cardiovascular and Renal Outcomes with Empagliflozin
in Heart Failure

M. Packer, S.D. Anker, J. Butler, G. Filippatos, S.J. Pocock, P. Carson, J. Januzzi, S. Verma, H. Tsutsui, M. Brueckmann, W. Jamal, K. Kimura, J. Schneid, C. Zeller, D. Cottone, E. Bocchi, M. Böhm, D.-J. Choi, V. Chopra, E. Chuquiure, N. Giannetti, S. Janssens, J. Zhang, J.R. González Juanatey, S. Kaul, H.-P. Brunner-La Rocca, B. Merkely, S.J. Nicholls, S. Perrone, I. Pina, P. Ponikowski, N. Sattar, M. Semlitsch, M.F. Semmler, J. Spinar, I. Squire, S. Taddei, C. Wanner, and F. Zannad, for the EMPEROR-Reduced Trial Investigators[†]

サブ解析

Empagliflozin投与**12**日目から統計学的有意に
心不全入院、悪化のイベントを低減



	Patients at risk				
	0	12	24	36	42
Placebo	1867	1852	1830	1811	1792
Empagliflozin	1863	1855	1845	1826	1815



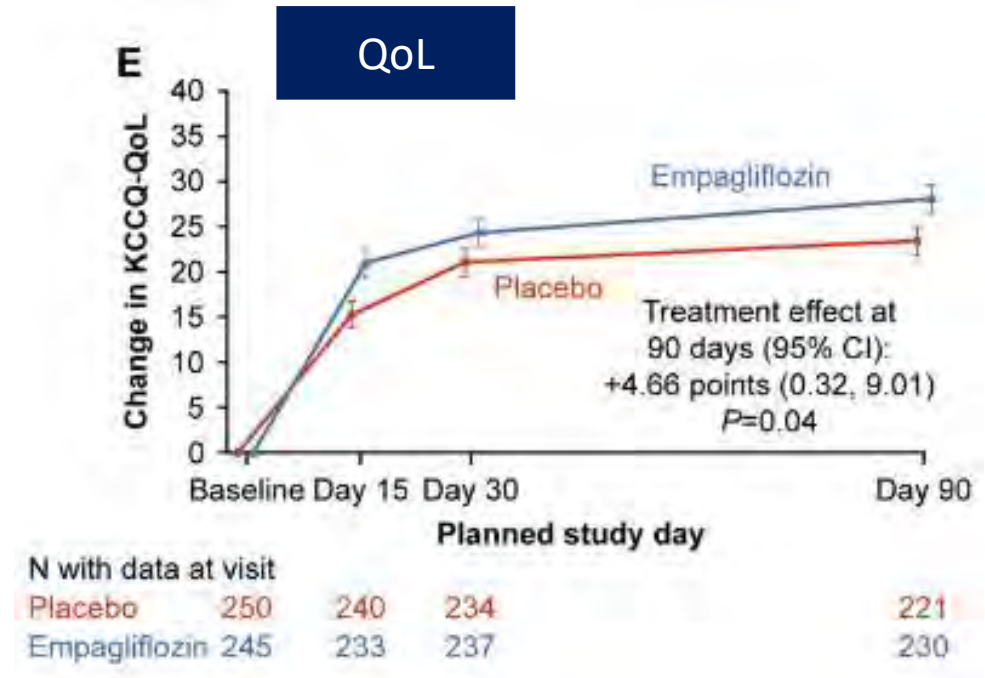
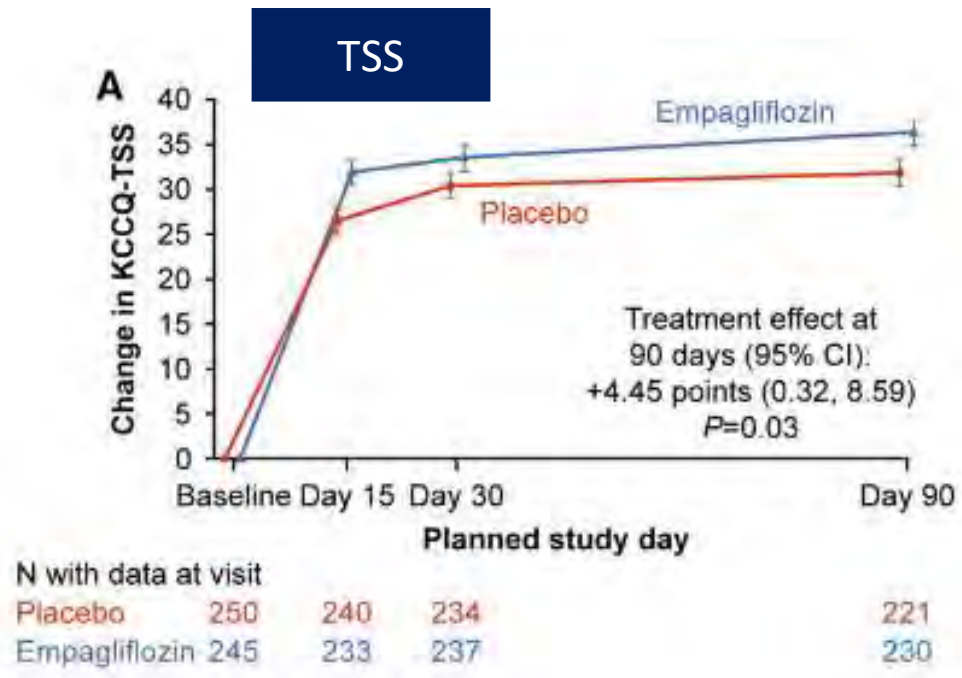
ORIGINAL RESEARCH ARTICLE



Effects of Empagliflozin on Symptoms, Physical Limitations, and Quality of Life in Patients Hospitalized for Acute Heart Failure: Results From the EMPULSE Trial

Mikhail N. Kosiborod¹, MD^{*}; Christiane E. Angermann², MD^{*}; Sean P. Collins, MD, MSc; John R. Teerlink³, MD; Piotr Ponikowski⁴, MD, PhD; Jan Biegus⁵, MD, PhD; Josep Comin-Colet⁶, MD, PhD; João Pedro Ferreira⁷, MD, PhD; Robert J. Mentz⁸, MD; Michael E. Nassif, MD; Mitchell A. Psotka, MD, PhD; Jasper Tromp, MD, PhD; Martina Brueckmann⁹, MD; Jonathan P. Blatchford¹⁰, CStat; Afshin Salsali, MD; Adriaan A. Voors¹¹, MD, PhD

急性心不全に効く (KCCQ) 15日目から90日まで



CONCLUSIONS: Initiation of empagliflozin in patients hospitalized for acute heart failure produced clinical benefit regardless of the degree of symptomatic impairment at baseline, and improved symptoms, physical limitations, and quality of life, with benefits seen as early as 15 days and maintained through 90 days.





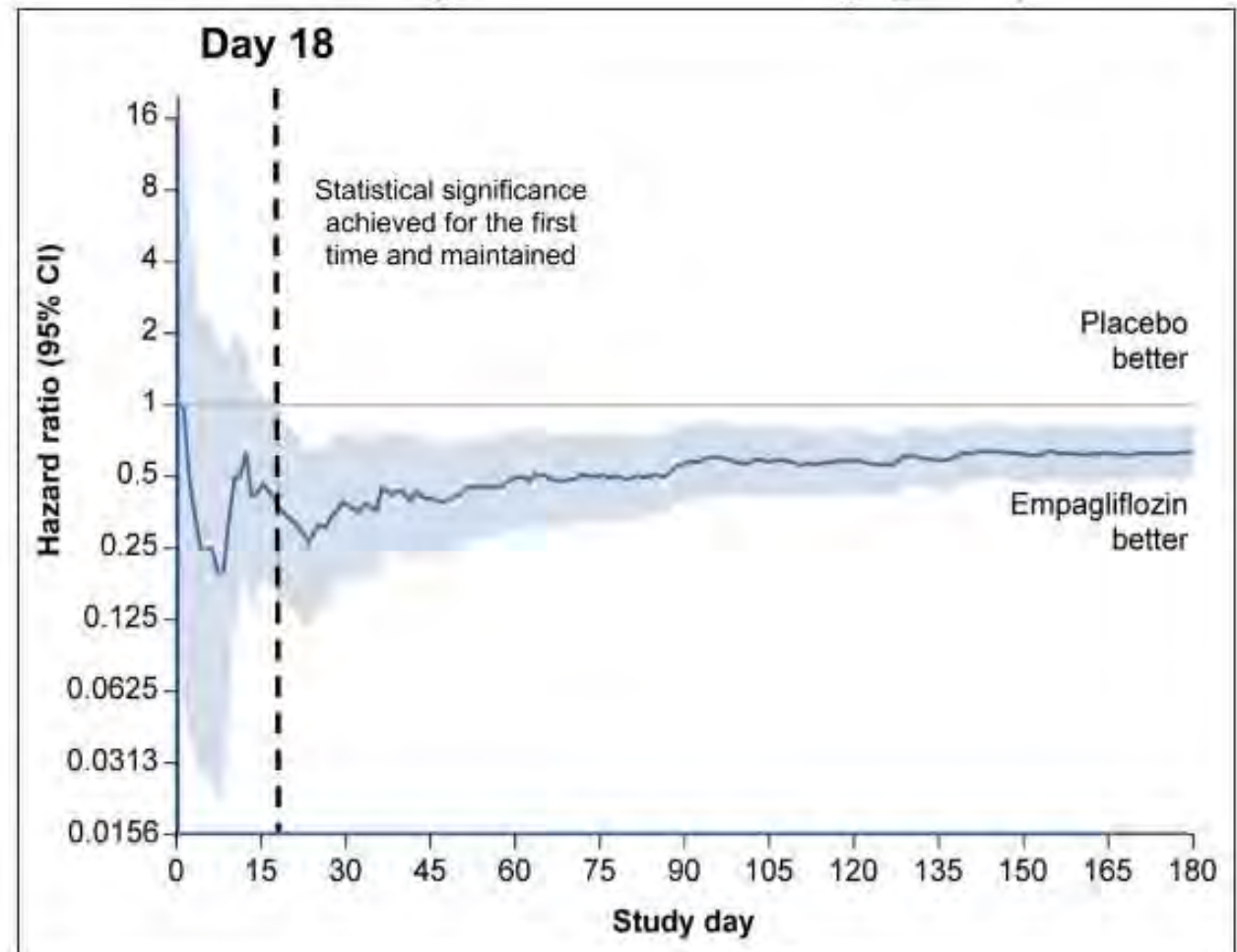
ORIGINAL RESEARCH ARTICLE

Effect of Empagliflozin on Worsening Heart Failure Events in Patients With Heart Failure and Preserved Ejection Fraction: EMPEROR-Preserved Trial

Milton Packer, MD, Javed Butler, MD, MPH, Faez Zannad, MD, PhD, Gerasimos Filippatos, MD, Joao Pedro Ferreira, MD, PhD, Stuart J. Pocock, PhD, Peter Carson, MD, Inder Anand, MD, Wolfram Doehner, MD, PhD, Markus Haass, MD, Michel Komajda, MD, Alan Miller, MD, Steen Pehrson, MD, John R. Teerlink, MD, Sven Schnaidt, MSc, Cordula Zeller, Dipl Math, Janet M. Schnee, MD, Stefan D. Anker, MD, PhD, and for the EMPEROR-Preserved Trial Study Group

Time of first statistical significance in time-to-first-event analysis of cardiovascular death, hospitalization for heart failure, or emergency or urgent heart failure visit requiring intravenous treatment for worsening heart failure.

18日で有意差がつく



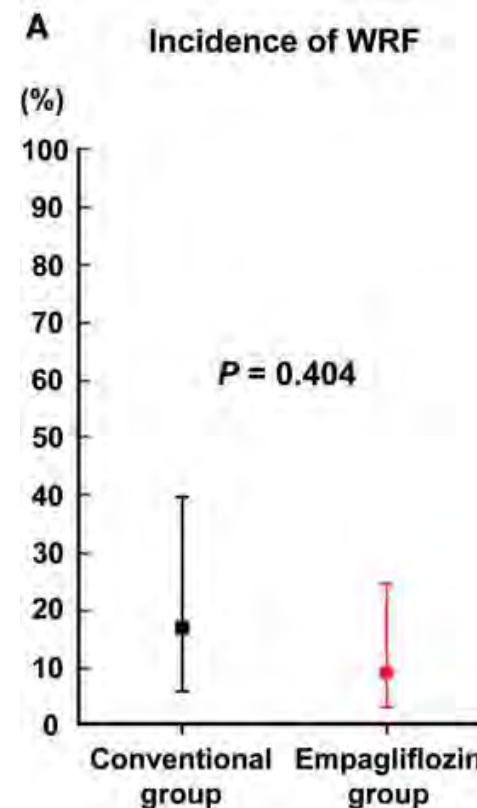
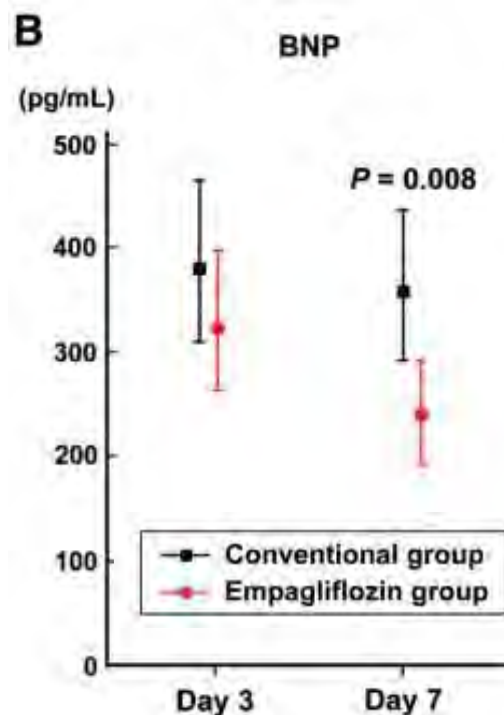
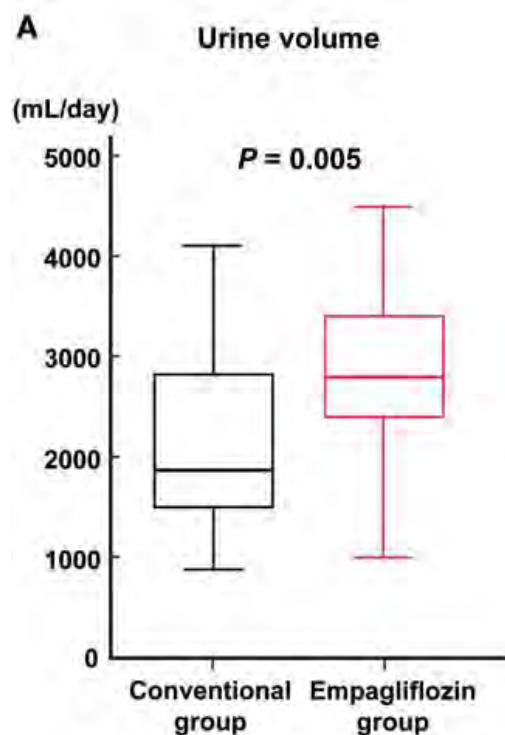
ORIGINAL ARTICLE

Effect of Empagliflozin as an Add-On Therapy on Decongestion and Renal Function in Patients With Diabetes Hospitalized for Acute Decompensated Heart Failure

A Prospective Randomized Controlled Study

Shunsuke Tamaki¹, MD, PhD; Takahisa Yamada, MD, PhD; Tatsuya Watanabe², MD, PhD; Takashi Morita³, MD, PhD; Yoshio Furukawa, MD, PhD; Masato Kawasaki⁴, MD; Atsushi Kikuchi, MD; Tsutomu Kawa⁵, MD; Masahiro Seo, MD; Makoto Abe, MD; Jun Nakamura, MD; Kyoko Yamamoto, MD; Kiyomi Kayama, MD; Masatsugu Kawahira, MD; Kazuya Tanabe, MD; Kei Fujikawa, MD; Masahisa Hata, MD; Yohei Fujita, MD; Yutaka Umayahara, MD, PhD; Satsuki Taniguchi⁶, MS; Shoji Sanada, MD, PhD; Ayumi Shintani, PhD, MPH; Masatake Fukunami, MD, PhD

急性心不全治療に Empagliflozin追加すると 腎機能悪化させずにうっ血改善



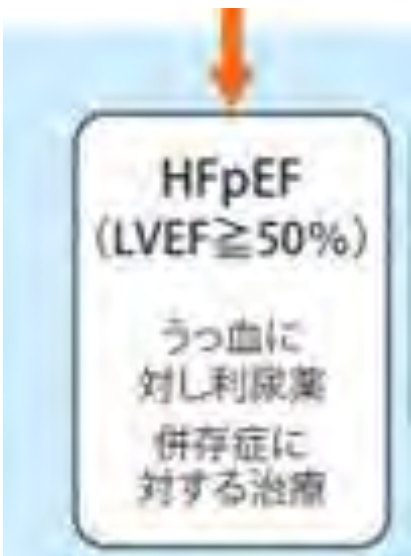
Prognostic Impact of Loop Diuretics in Patients With Chronic Heart Failure

– Effects of Addition of Renin-Angiotensin-Aldosterone System Inhibitors and β -Blockers –

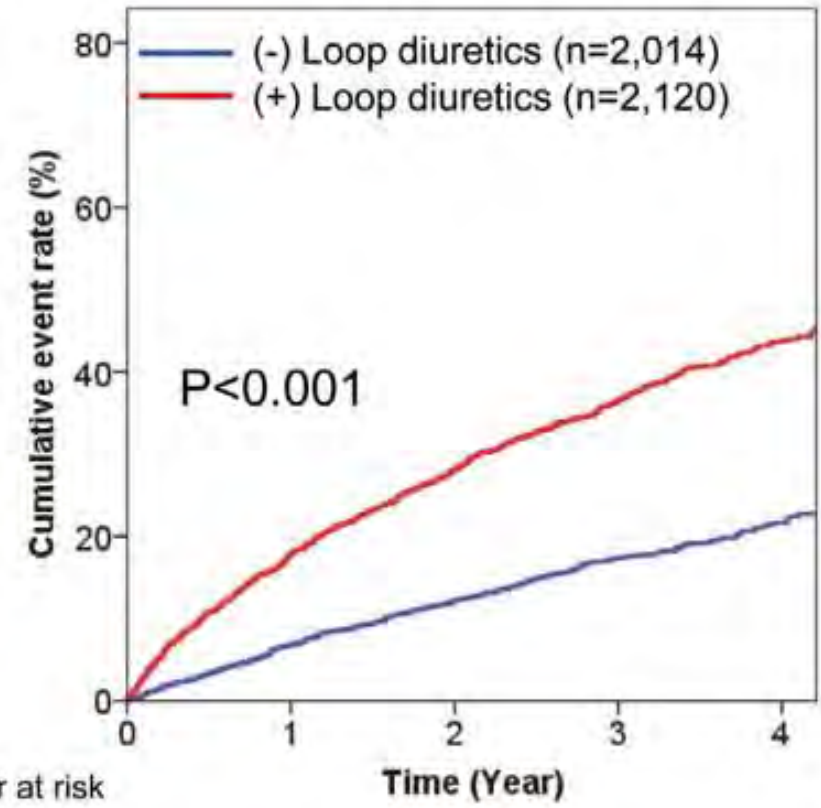
Masanobu Miura, MD, PhD; Koichiro Sugimura, MD, PhD; Yasuhiko Sakata, MD, PhD; Satoshi Miyata, PhD; Soichiro Tadaki, MD; Takeshi Yamauchi, MD; Takeo Onose, MD; Kanako Tsuji, MD; Ruri Abe, MD; Takuya Oikawa, MD; Shintaro Kasahara, MD; Kotaro Nochioka, MD, PhD; Jun Takahashi, MD, PhD; Hiroaki Shimokawa, MD, PhD on behalf of the CHART-2 Investigators

SGLT2阻害薬は腎機能悪化させず、RAAS系刺激せず
ループ利尿薬使用、量多いと予後不良

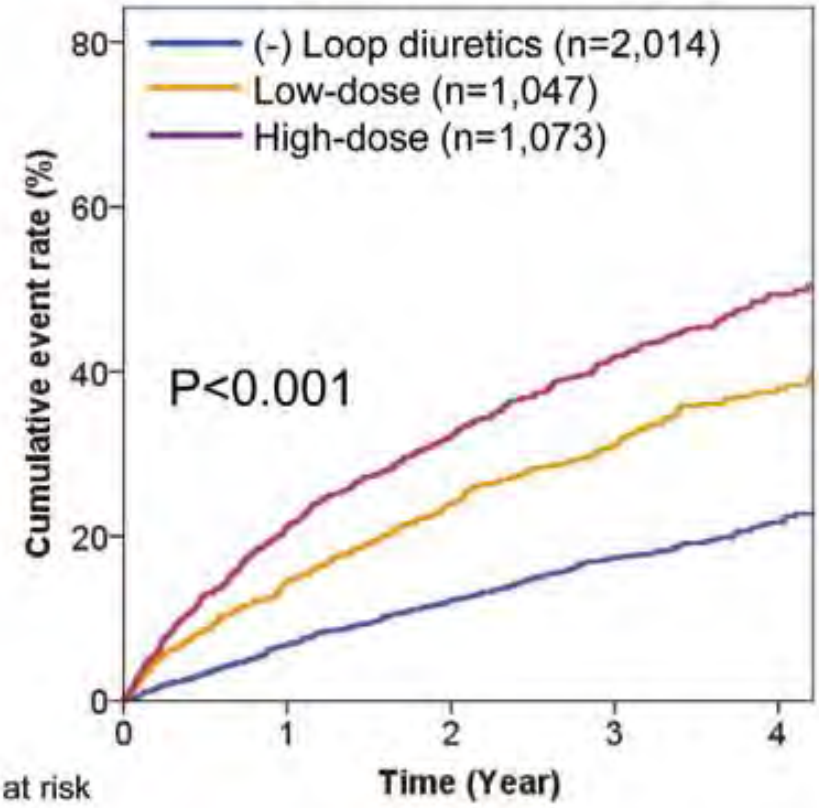
2021年9月10日更新
2021年3月26日発行
日本循環器学会 / 日本心不全学会合同ガイドライン
2021年 JCS/JHFS ガイドライン フォーカスアップデート版
急性・慢性心不全診療
JCS/JHFS 2021 Guideline Focused Update on Diagnosis and Treatment of Acute and Chronic Heart Failure
「急性・慢性心不全診療ガイドライン (2017年改訂版)」からあらたな知見を基と、フォーカスアップデートとして作成した。



A



B

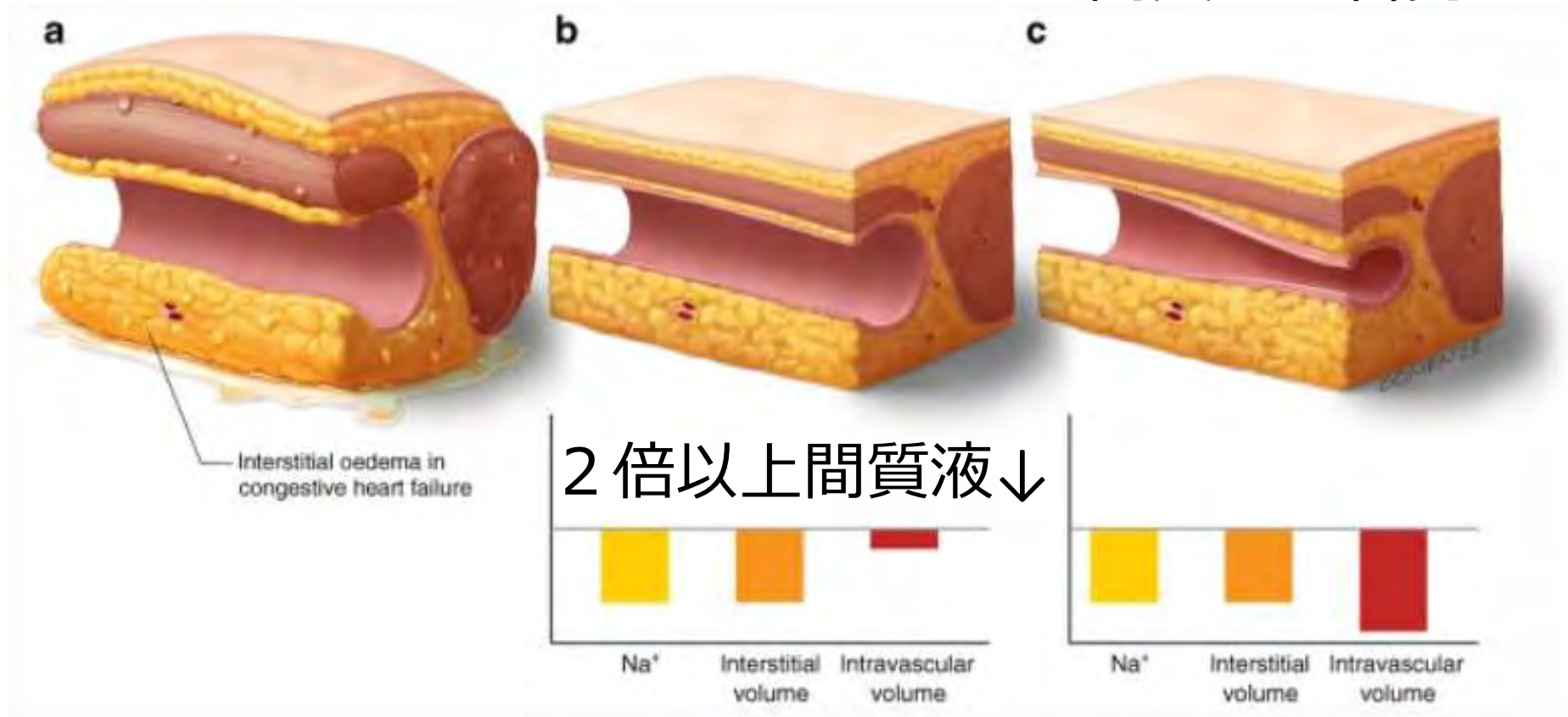


Why do SGLT2 inhibitors reduce heart failure hospitalization? A differential volume regulation hypothesis

血管内脱水を起こしにくい

SGLT2iでは
間質 > 血管内

ループ利尿薬
間質 < 血管内



ORIGINAL RESEARCH ARTICLE

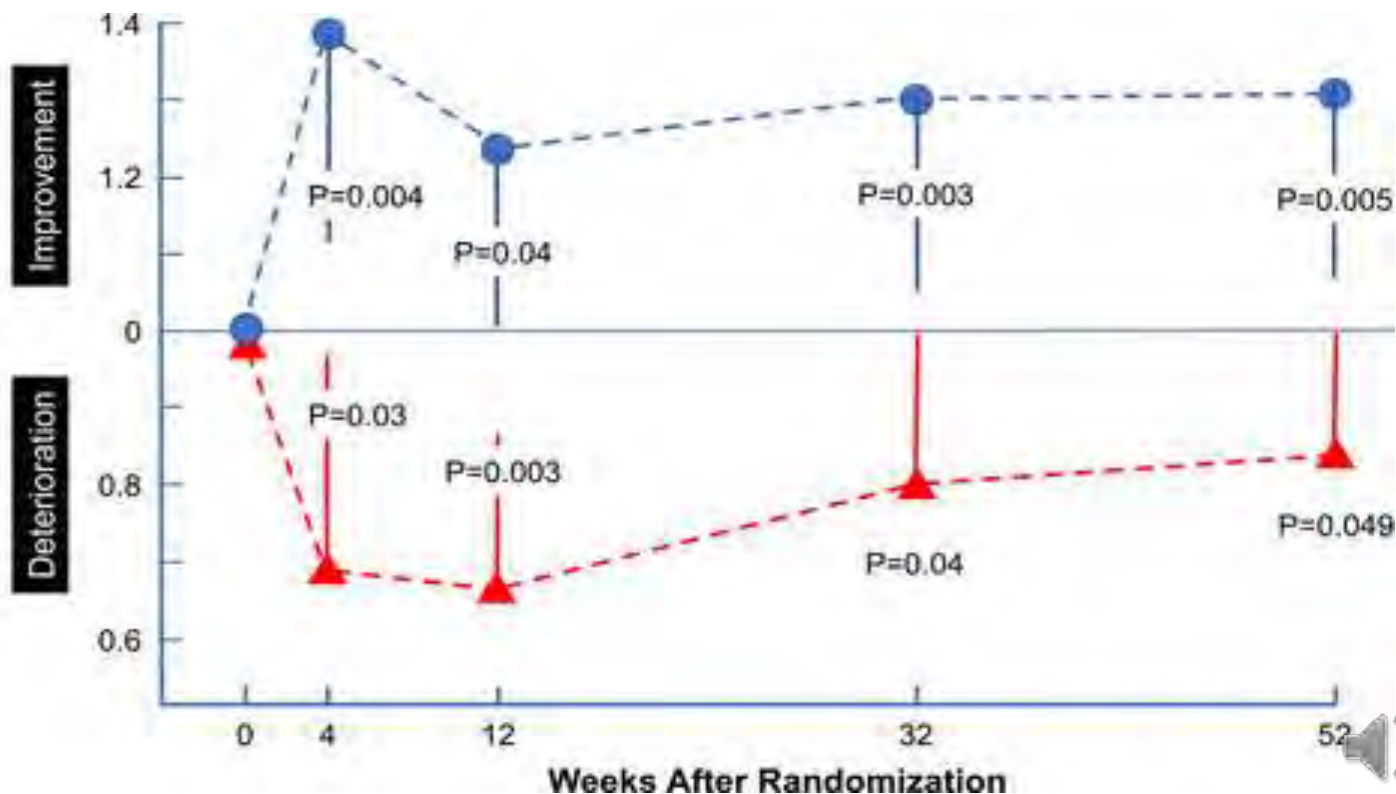
Effect of Empagliflozin on the Clinical Stability of Patients With Heart Failure and a Reduced Ejection Fraction

The EMPEROR-Reduced Trial

Milton Packer, MD , Stefan D. Anker, MD, PhD , Javed Butler, MD, MPH , Gerasimos Filippatos, MD , João Pedro Ferreira, MD, PhD , Stuart J. Pocock, PhD, Peter Carson, MD, Inder Anand, MD , Wolfram Doehner, MD, Markus Haass, MD, Michel Komajda, MD, Alan Miller, MD, Steen Pehrson, MD, John R. Teerlink, MD , Martina Brueckmann, MD, Waheed Jamal, MD, Cordula Zeller, Dipl Math, Sven Schnaidt, MSc, Faiez Zannad, MD, PhD , and for the EMPEROR-Reduced Trial Committees and Investigators

4週～1年で有意差

Odds ratio for empagliflozin : placebo
for changes in NYHA functional class



Sodium-Glucose Cotransporter-2 Inhibitors in Patients With Heart Failure

A Systematic Review and Meta-analysis

Ann Intern Med 2022 Apr 12 doi.10.7326/M24-4284

SGLT2阻害薬は心不全入院リスクを長期にわたり有意に抑制
6カ月後**37%**、1年後は**32%**、**2年後**は**26%**

予後不良患者においてリスク差がより大、心保護効果が顕著
心不全の診断後 **1** 年目からの処方
他疾患で入院中に心不全を診断

性器感染症の相対リスクが2.69と高い



Gliflozins in the Management of Cardiovascular Disease

Eugene Braunwald, M.D.

May 26, 2022

N Engl J Med 2022; 386:2024-2034

DOI: 10.1056/NEJMra2115011

「変わる」
糖尿病薬→心腎治療薬

- 1) Phlorizinはリンゴ樹皮抽出物、尿細管でSGLT2阻害→ブドウ糖再吸収阻害→尿糖排出
- 2) 経口SGLT2阻害薬は田辺製薬が開発、RCTで心血管リスク確認→心腎保護確認
- 3) EMPA-REG2015で心血管疾患14%減、2-3週で効果発現、心不全入院35%減
- 4) SGLT2阻害薬で心血管イベント減少、心不全入院はすべての試験で減少
- 5) SGLT2阻害薬の心腎保護効果は血糖と無関係、HFpEFにも効果あり (EF25-65%)
- 6) SGLT2阻害薬は腎機能無関係に透析、腎移植、腎死減 (RR0.67)、初期GFR dipあり
- 7) SGLT2阻害→尿細管Na↑→緻密班が輸入細動脈縮小→過剰ろ過↓→腎改善
- 8) 心臓への作用機序不明、ミトコンドリア機能改善？心筋Na濃度減？炎症軽減？異所性脂肪減？
- 9) 副作用：陰部、尿路感染症、血糖正常ケトアシドーシス、足趾切断？
- 10) SGLT2阻害薬で心房細動/粗動2割減、心室性不整脈、突然死3割減
- 11) SGLT2阻害薬とGLP-1受容体作動薬併用は相乗効果あり



Gliflozins in the Management of Cardiovascular Disease

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SGLT2阻害薬下の心腎連関

Renal Actions

SGLT2阻害



尿細管Na増



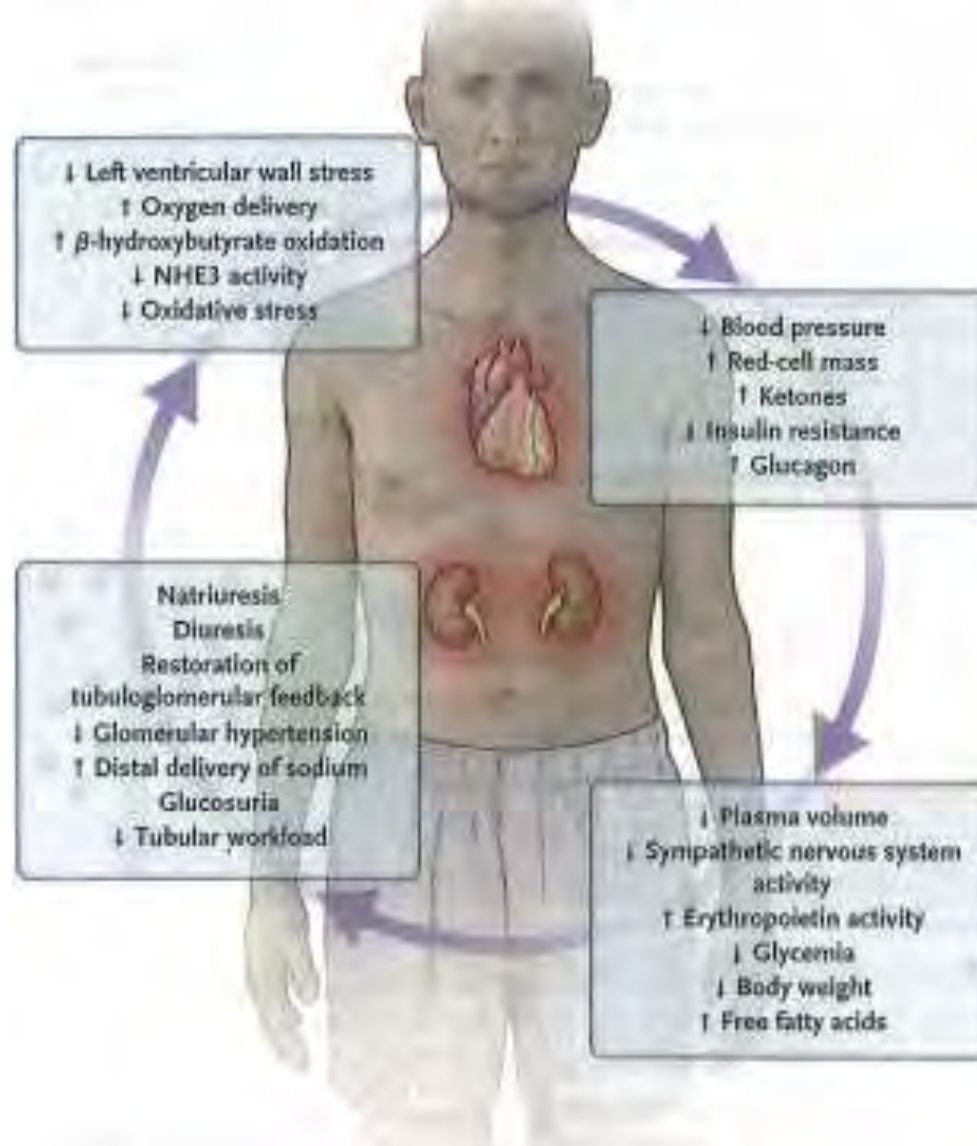
緻密斑が輸入細動脈縮小



過剰ろ過減



腎改善



Cardiac Actions ?

ケトン体を介する
ミトコンドリア機能改善

心筋細胞内Na濃度改善

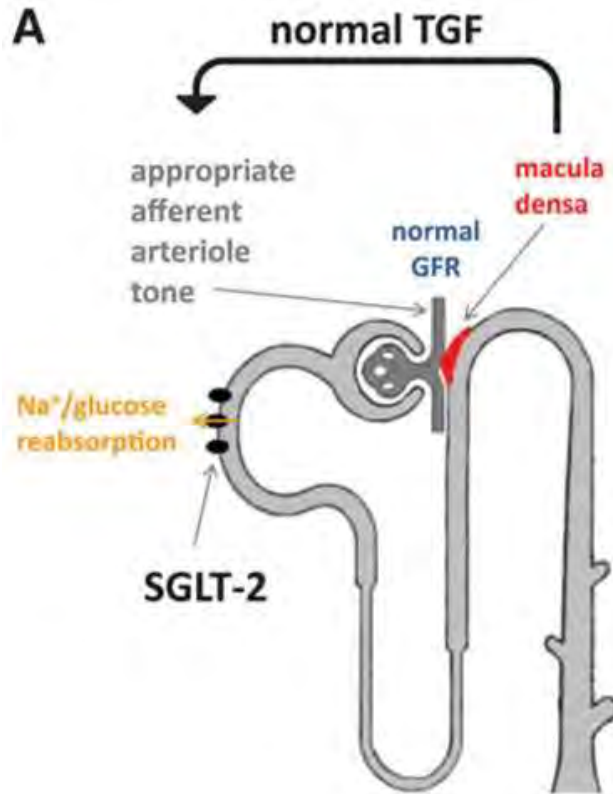
炎症反応改善

異所性脂肪減



ORIGINAL ARTICLE

Renal Hemodynamic Effect of Sodium-Glucose Cotransporter 2 Inhibition in Patients With Type 1 Diabetes Mellitus



Normal physiology

尿細管糸球体フィードバック

TGF (Tubuloglomerular feedback)

尿細管は上行脚終末部で糸球体に戻る走行、輸入細動脈に近接マクラデンサ細胞 尿細管NaCl濃度感知
輸入細動脈にフィードバック

NaCl排泄の厳格化

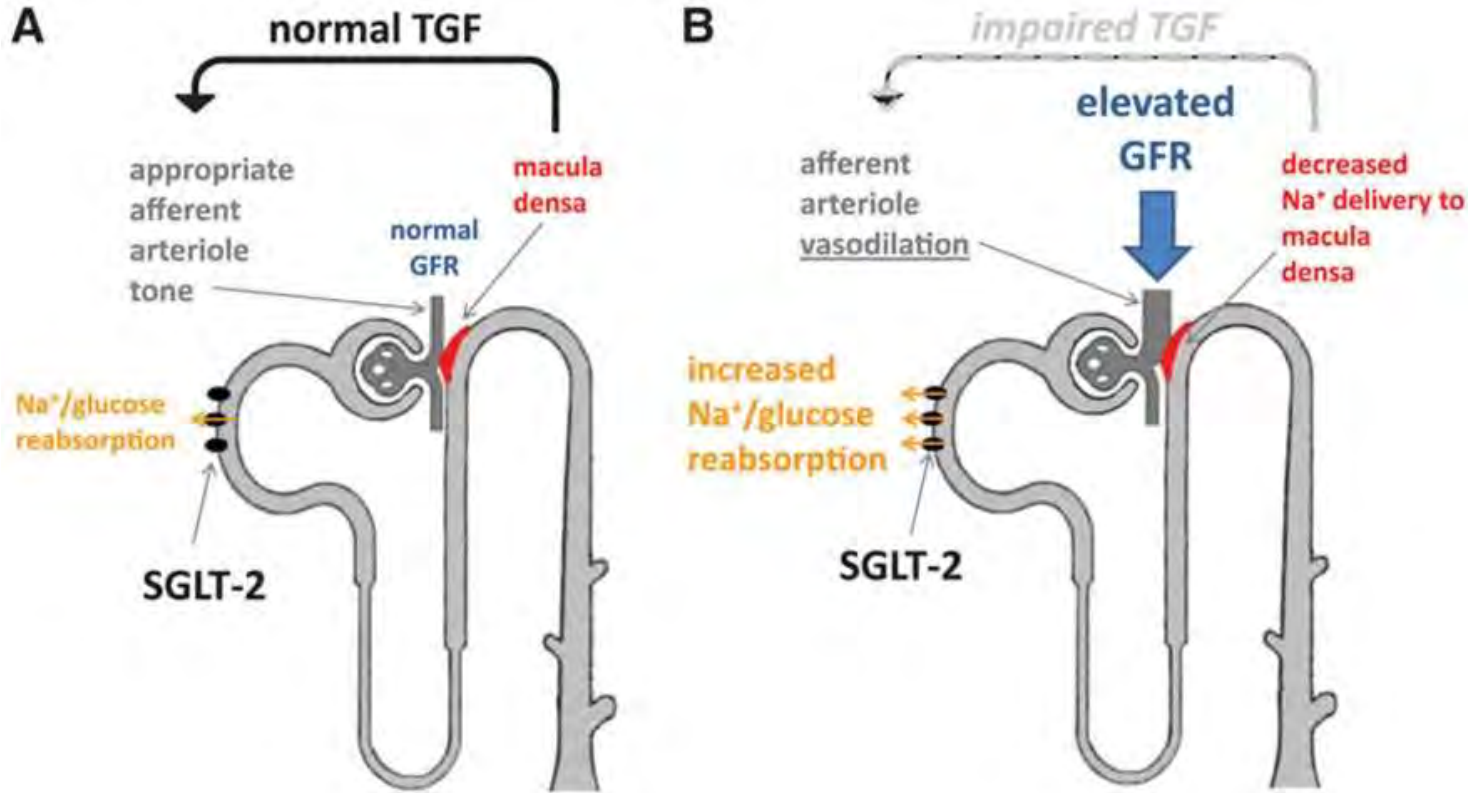
尿細管NaCl濃度低下はGFR低下と認識
輸入細動脈拡張し、NaCl排出を促進
逆ならば輸入細動脈収縮し、排泄抑制
生命の恒常性維持システム



ORIGINAL ARTICLE

Renal Hemodynamic Effect of Sodium-Glucose Cotransporter 2 Inhibition in Patients With Type 1 Diabetes Mellitus

尿細管糸球体フィードバック



Normal physiology

Hyperfiltration in early stages of diabetic nephropathy

糖尿病腎

糸球体から濾過されるグルコース増加
再吸収するSGLT2活性上昇
グルコースとNaCl再吸収増加

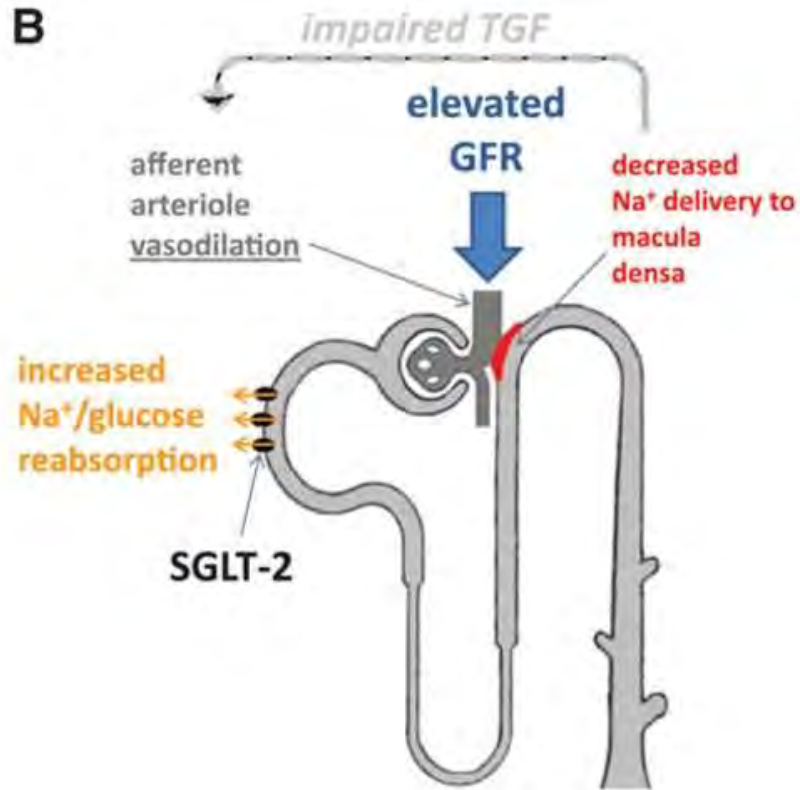
尿細管NaCl濃度低下
マクラデンサ細胞がGFR低下と認識
輸入細動脈拡張
糸球体Hyperfiltration、糸球体内圧増
糸球体内皮障害



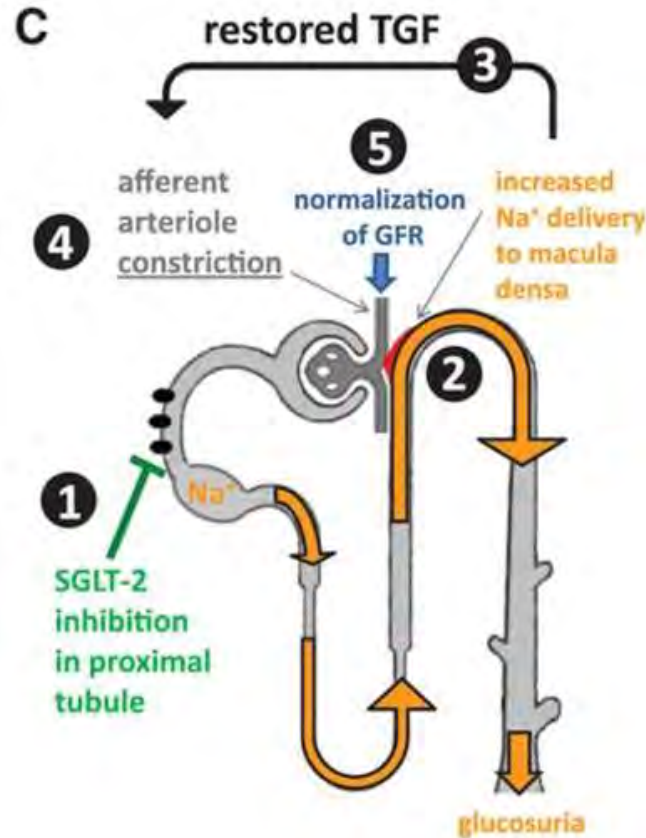
ORIGINAL ARTICLE

Renal Hemodynamic Effect of Sodium-Glucose Cotransporter 2 Inhibition in Patients With Type 1 Diabetes Mellitus

尿細管糸球体フィードバック



Hyperfiltration in early stages of diabetic nephropathy



SGLT-2 inhibition reduces hyperfiltration via TGF

SGLT2阻害薬

近位尿細管グルコースNaCl再吸収抑制

尿細管内NaCl濃度是正

TGF是正

糸球体内圧低下

糸球体内皮障害予防

TGF是正は糸球体到達血液量減

急性的なGFR低下

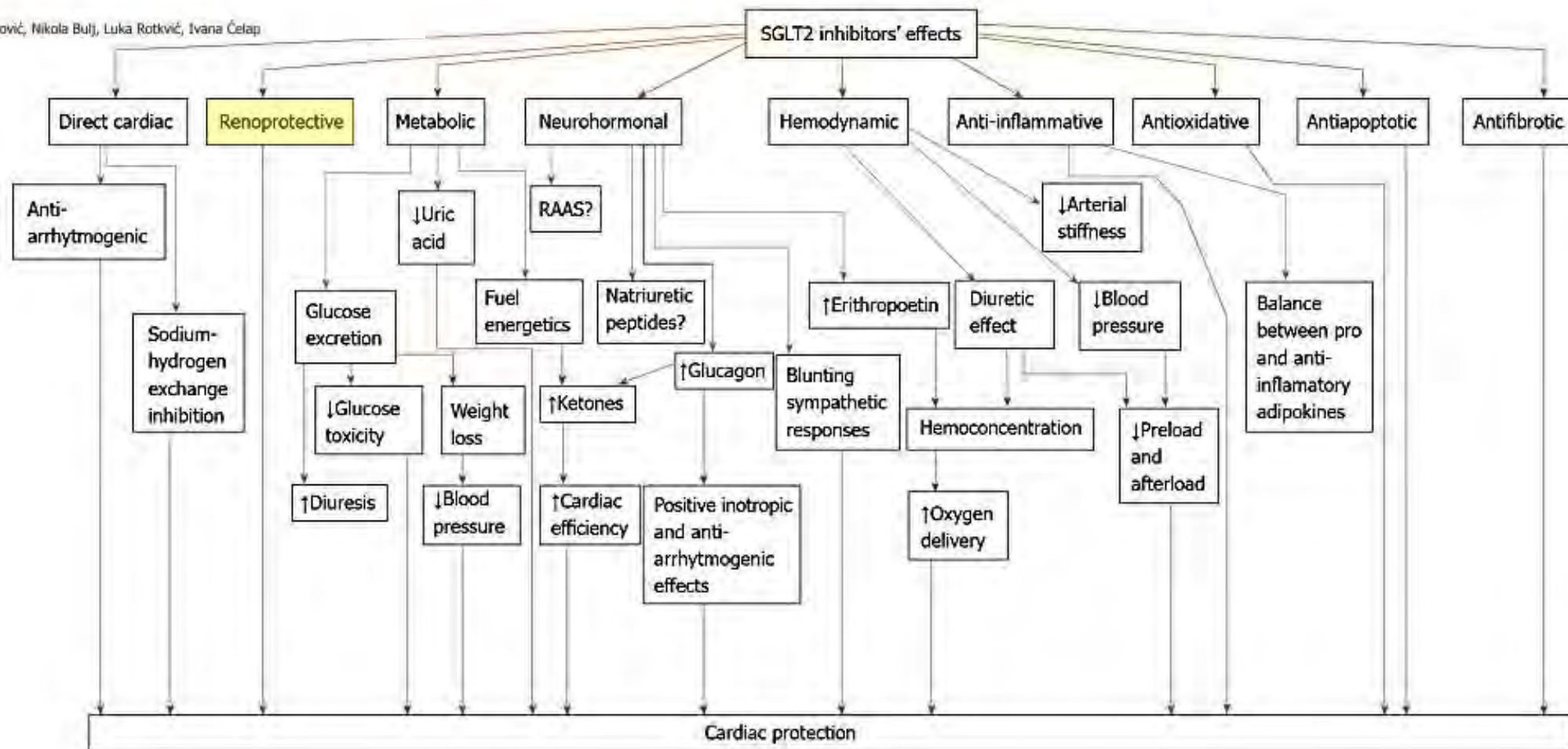
慢性的には腎保護



多様なメカニズムの提唱はあるが... **腎** 保護が主体か

Sodium-glucose cotransporter 2 inhibitors' mechanisms of action in heart failure

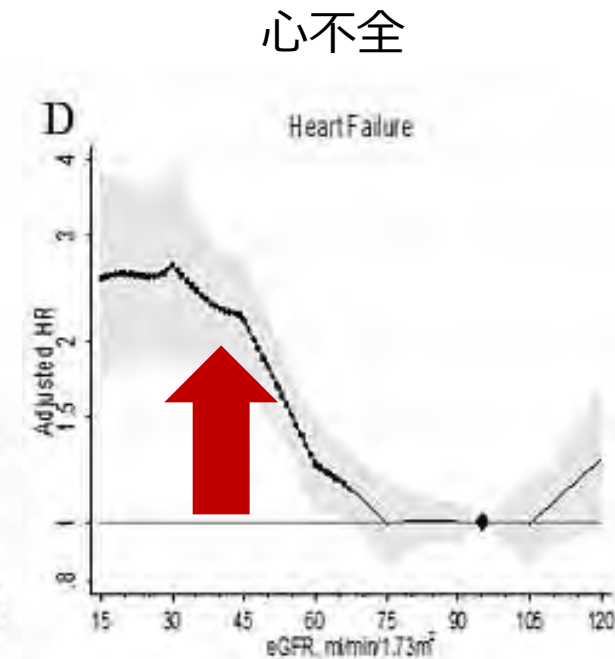
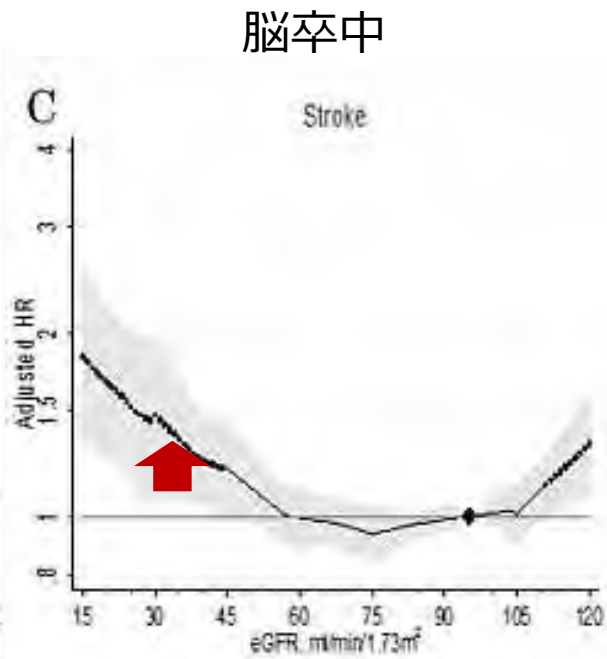
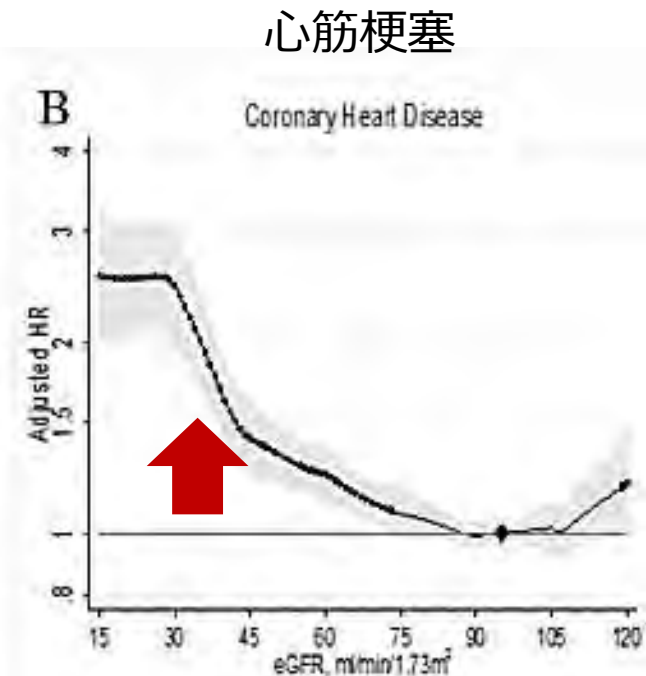
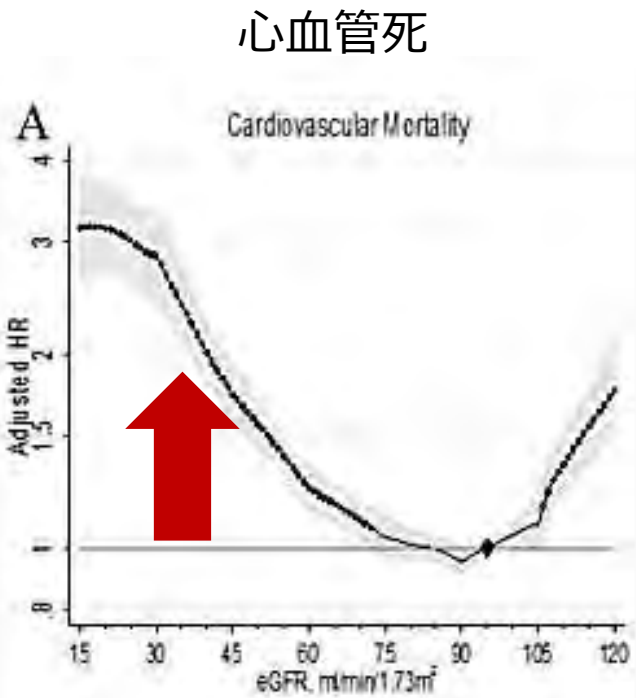
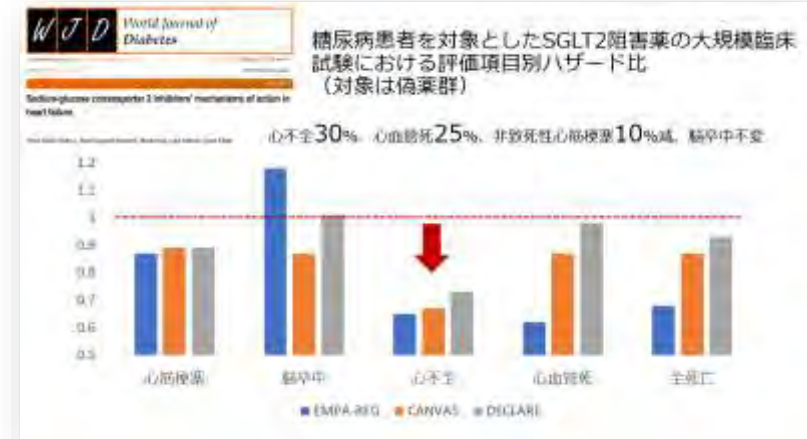
Petra Grubić Rotkvić, Maja Cigrovski Berković, Nikola Bulj, Luka Rotkvić, Ivana Čelap



Kidney measures beyond traditional risk factors for cardiovascular prediction: A collaborative meta-analysis

一般人コホートを対象にしたeGFR別疾病発生頻度調整ハザード比

腎機能低下で心不全 > 心筋梗塞 > 脳卒中



Short-Term Change in eGFR and Risk of Cardiovascular Events

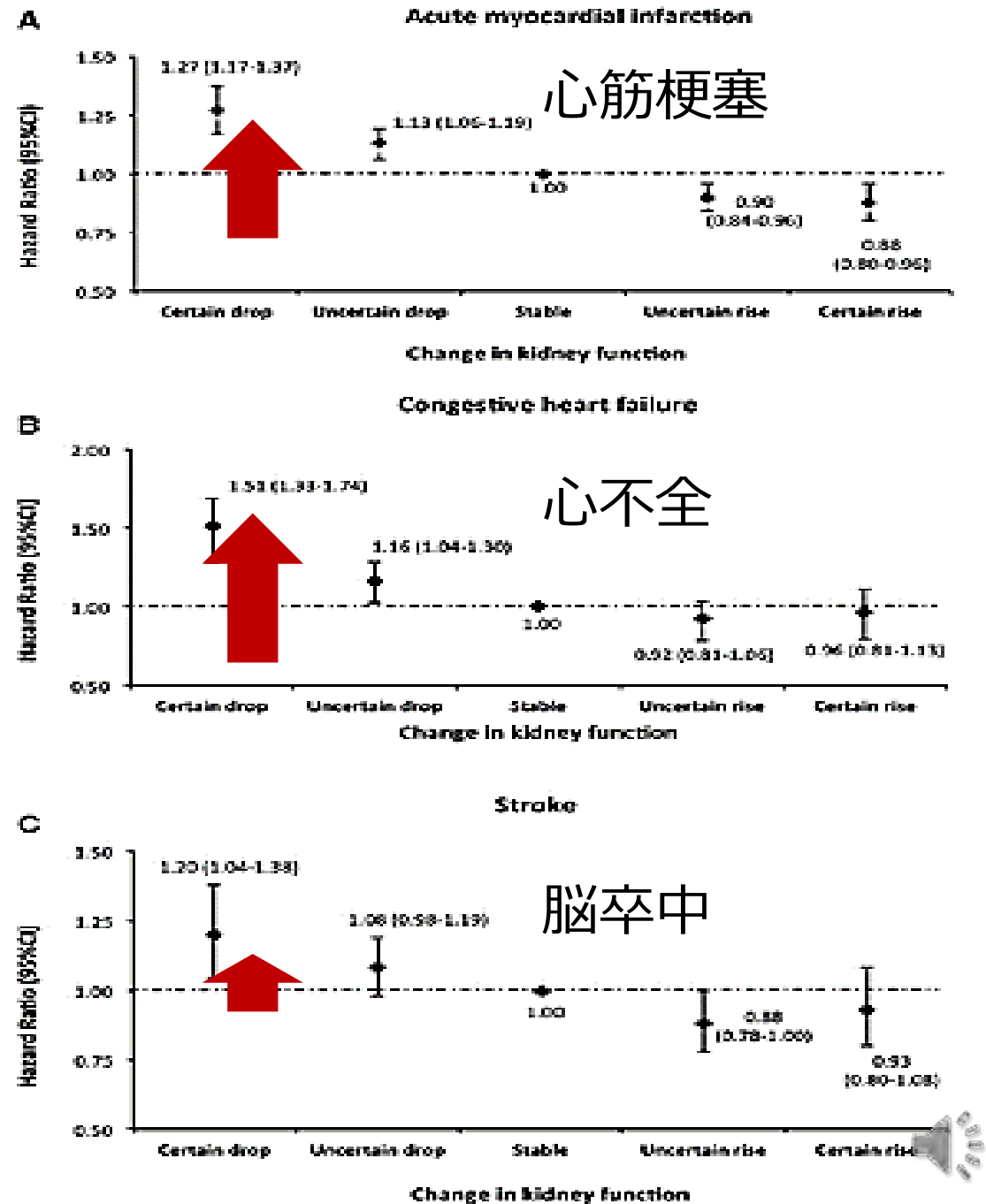
Tanvir Chowdhury Turin, MD; Matthew T. James, MD; Min Jun, PhD; Marcello Tonelli, MD; Joseph Coresh, MD; Braden J. Manns, MD; Brenda R. Hemmelgarn, MD

J Am Heart Assoc. 2014;3:e000997. <https://doi.org/10.1161/JAHA.114.000997>

eGFRの変化度と心筋梗塞、心不全、脳卒中の発生頻度ハザード比

ベースラインから25%変化を閾値として変化を著減、微減、安定、微増、著増の5群に分類

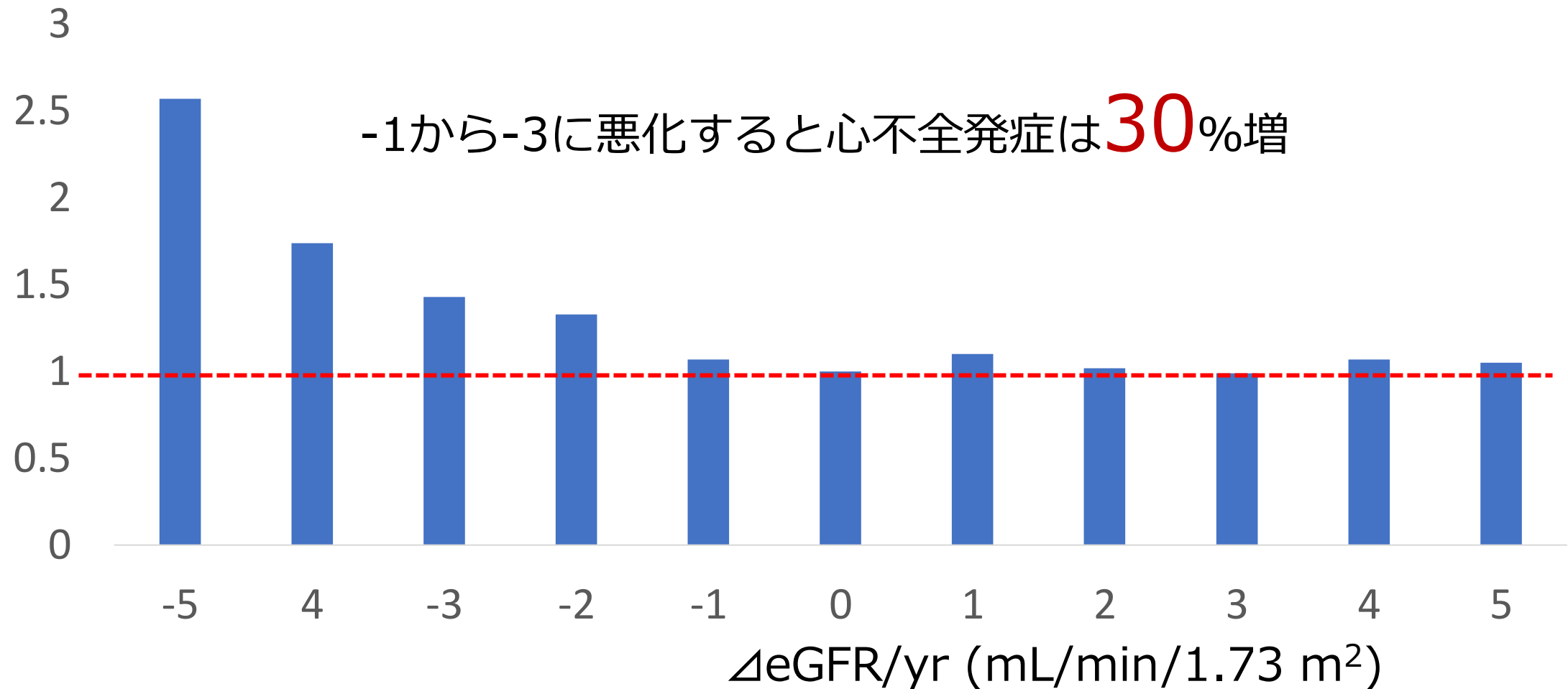
eGFR低下速度大になると
心不全 > 心筋梗塞 > 脳卒中
1.51 1.27 1.20



Magnitude of rate of change in kidney function and future risk of cardiovascular events

Int J Cardiol. 2016 Jan 1;202:657-65. doi: 10.1016/j.ijcard.2015.09.090.

一般人集団におけるeGFR低下速度と心不全発症ハザード比





ORIGINAL RESEARCH ARTICLE

Efficacy of Dapagliflozin on Renal Function and Outcomes in Patients With Heart Failure With Reduced Ejection Fraction

Results of DAPA-HF

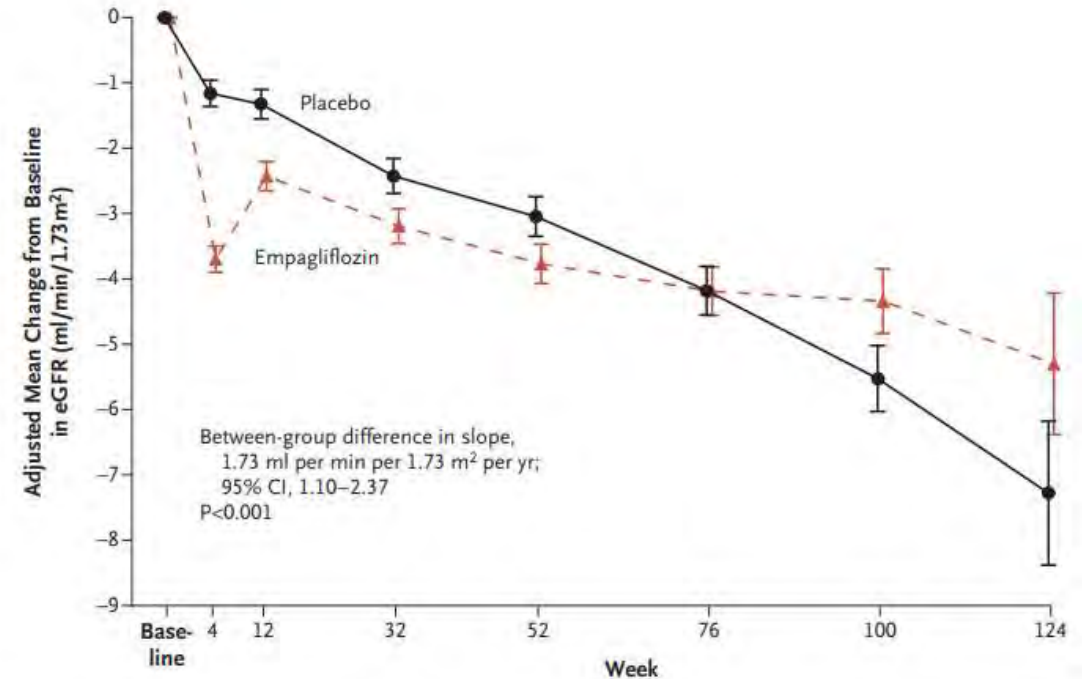
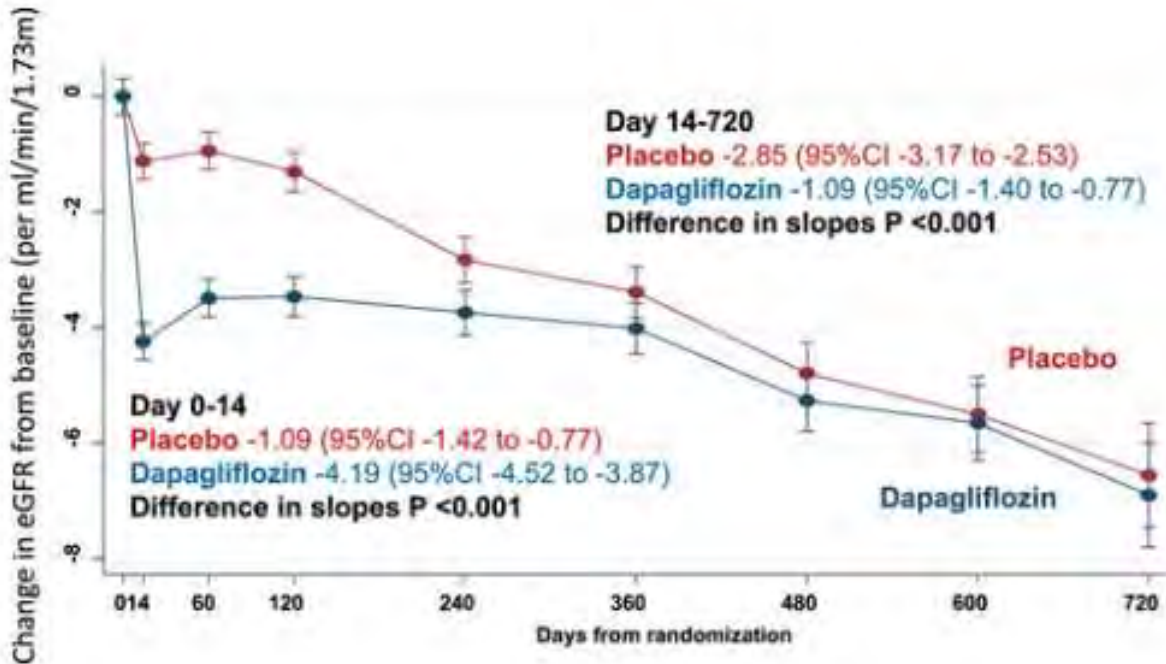
△eGFRを
 変える薬



Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure

M. Packer, S.D. Anker, J. Butler, G. Filippatos, S.J. Pocock, P. Carson, J. Januzzi, S. Verma, H. Tansu, M. Budde, W. Jamal, K. Gheera, J. Solomon, C. Zeller, D. Cotton, E. Pocock, M. Basso, D. J. V. Chapp, E. Chagnac, H. Guarnieri, S. Janssens, J. Zhang, J. W. Gonzalez-Juanatey, S. Kasl, H.-P. Brunner, G. Wozniak, E. Mendy, S.J. Pocock, S. Pocock, J. Pocock, P. Pocock, N. Sattar, M. Ström, M.-P. Semmler, J. Sironi, I. Soubrier, S. Taddei, C. Wanner, and F. Zannad for the EMPEROR-Reduced Trial Investigators*

DAPA – HFとEMPEROR-ReducedにおけるSGLT2阻害薬と偽薬での腎機能低下率



No. at Risk
 Placebo
 Empagliflozin

	1792	1765	1683	1500	1146	745	343	76
	1799	1782	1720	1554	1166	753	356	80



Efficacy of Dapagliflozin on Renal Function and Outcomes in Patients With Heart Failure With Reduced Ejection Fraction

Results of DAPA-HF

一次評価項目におけるDAPAGLIFLOZIN投与群の偽薬群に対するハザード比

eGFR低い群で
効果が増強？

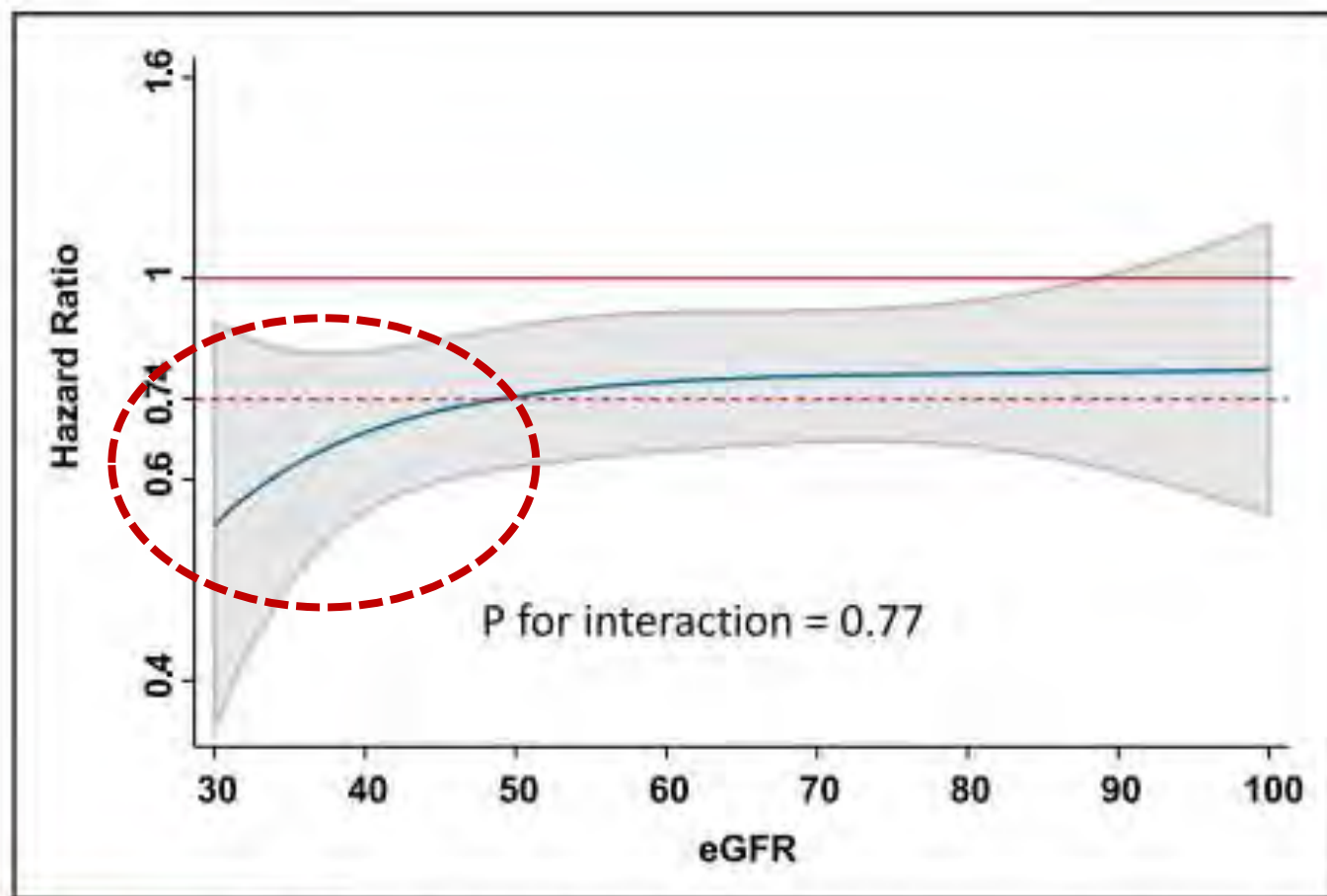


Figure 1. Effect of dapagliflozin on the primary outcome by eGFR at baseline.





Effects of empagliflozin on the urinary albumin-to-creatinine ratio in patients with type 2 diabetes and established cardiovascular disease: an exploratory analysis from the EMPA-REG OUTCOME randomised, placebo-controlled trial

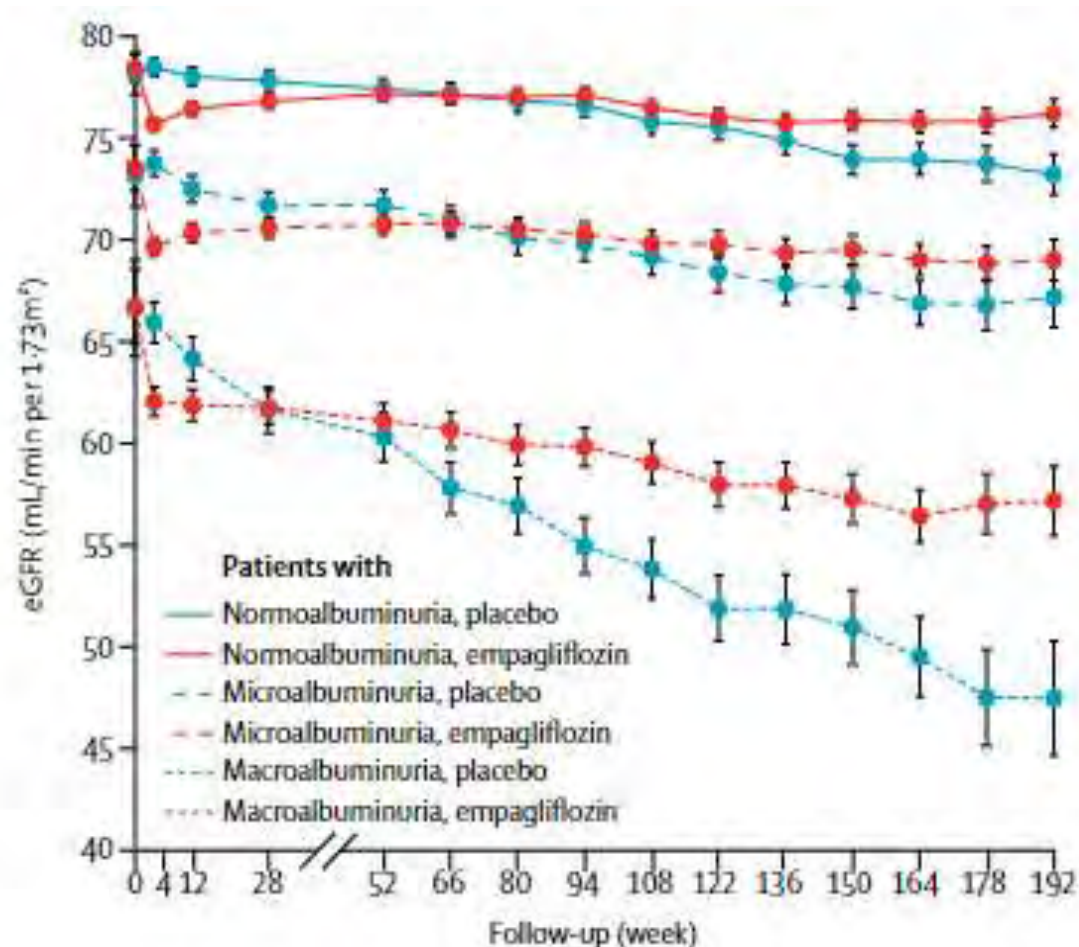
Daniil Z. Cherepanov, Benedek Zimanyi, Silvio Z. Inzucchi, Audrey Kotko-Welton, Michaela Metzke, Matthias von Eyben, Christoph Wanner

Lancet Diabetes Endocrinol 2017;

5: 610-21

尿中アルブミンがあってもなくても
 Δ eGFRは改善する

初期にいったんGFR低下



アルブミン尿なし

微量アルブミン尿

アルブミン尿++





SGLT2阻害薬は腎臓を護るから心不全が少ない



Gliflozins in the Management of Cardiovascular Disease

Eugene Braunwald, M.D.

May 26, 2022

N Engl J Med 2022; 386:2024-2034

DOI: 10.1056/NEJMra2115011

「変わる」
糖尿病薬→心腎治療薬

- 1) Phlorizinはリンゴ樹皮抽出物、尿細管でSGLT2阻害→ブドウ糖再吸収阻害→尿糖排出
- 2) 経口SGLT2阻害薬は田辺製薬が開発、RCTで心血管リスク確認→心腎保護確認
- 3) EMPA-REG2015で心血管疾患14%減、2-3週で効果発現、心不全入院35%減
- 4) SGLT2阻害薬で心血管イベント減少、心不全入院はすべての試験で減少
- 5) SGLT2阻害薬の心腎保護効果は血糖と無関係、HFpEFにも効果あり (EF25-65%)
- 6) SGLT2阻害薬は腎機能無関係に透析、腎移植、腎死減 (RR0.67)、初期GFR dipあり
- 7) SGLT2阻害→尿細管Na↑→緻密班が輸入細動脈縮小→過剰ろ過↓→腎改善
- 8) **心臓への作用機序不明**、ミトコンドリア機能改善？心筋Na濃度減？炎症軽減？**異所性脂肪減？**
- 9) 副作用：陰部、尿路感染症、血糖正常ケトアシドーシス、足趾切断？
- 10) SGLT2阻害薬で心房細動/粗動2割減、心室性不整脈、突然死3割減
- 11) SGLT2阻害薬とGLP-1受容体作動薬併用は相乗効果あり



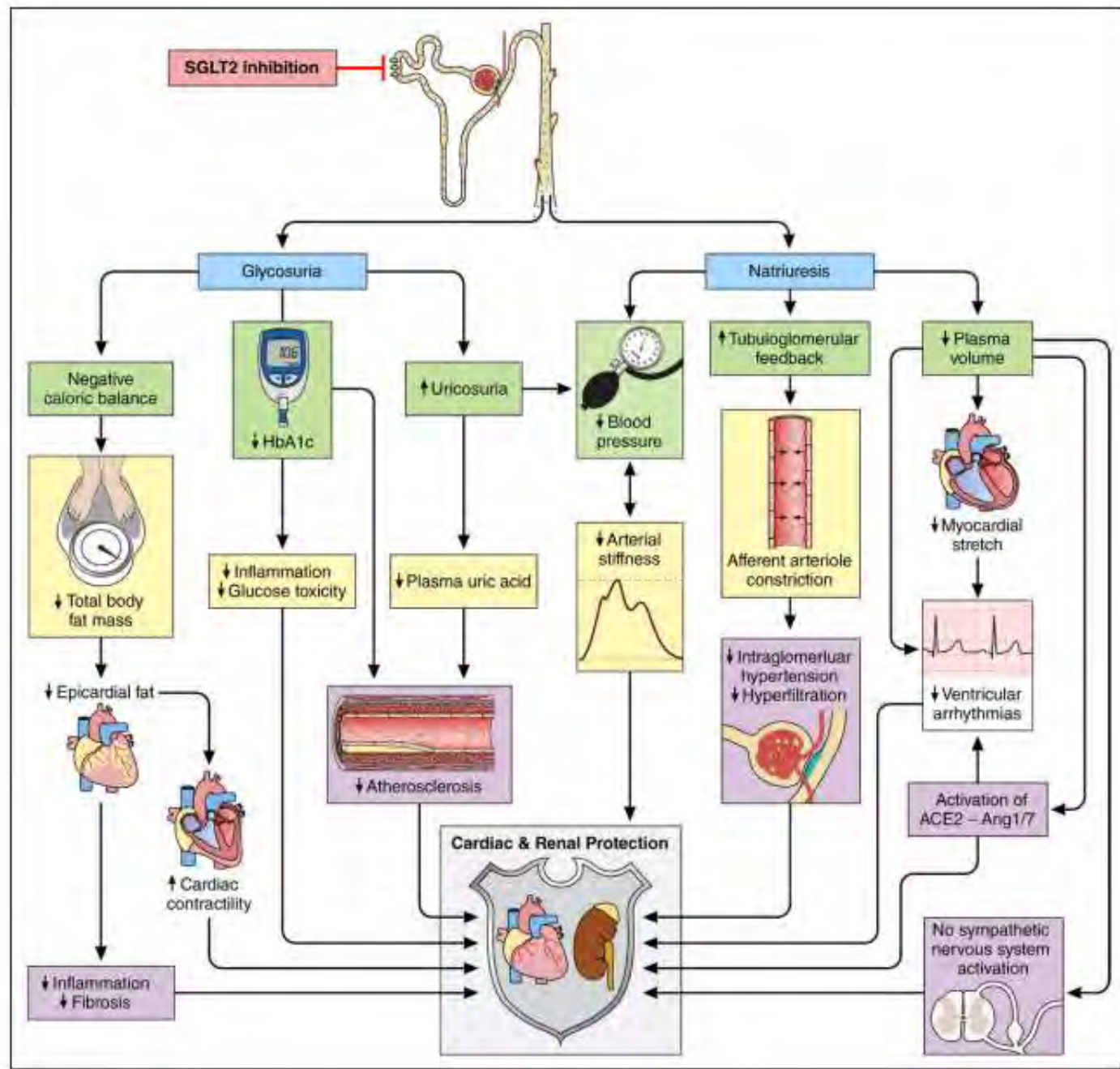
2つの排泄増

Na排泄増加

血压
循環血漿量
糸球体内圧

尿糖排泄増加

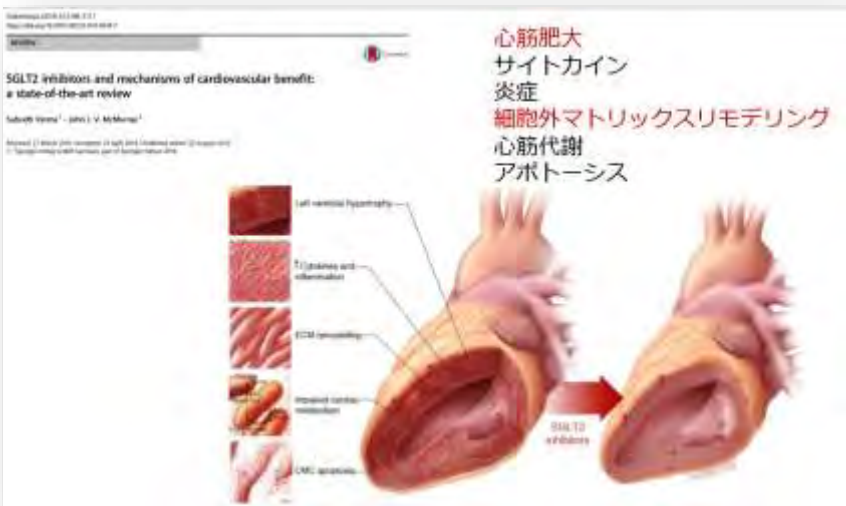
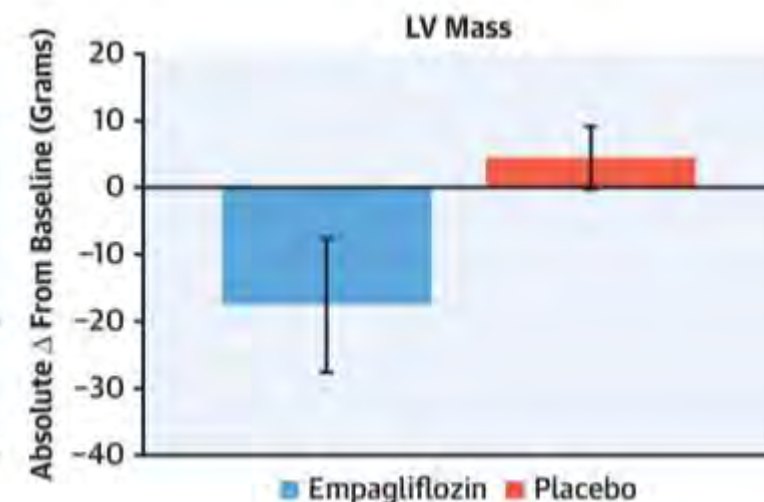
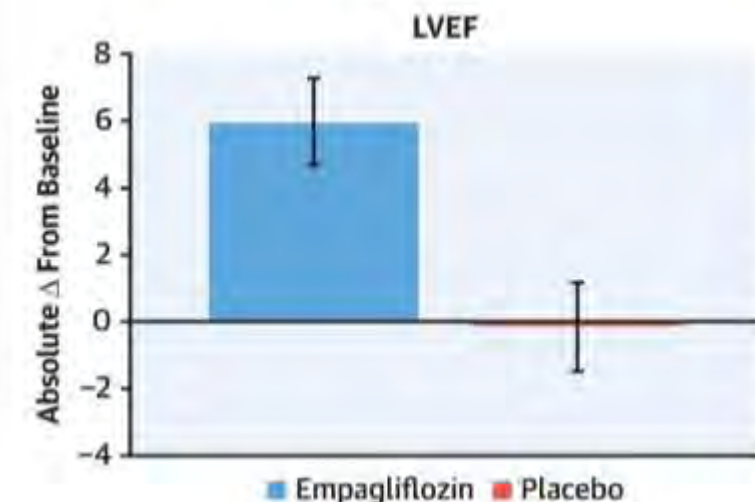
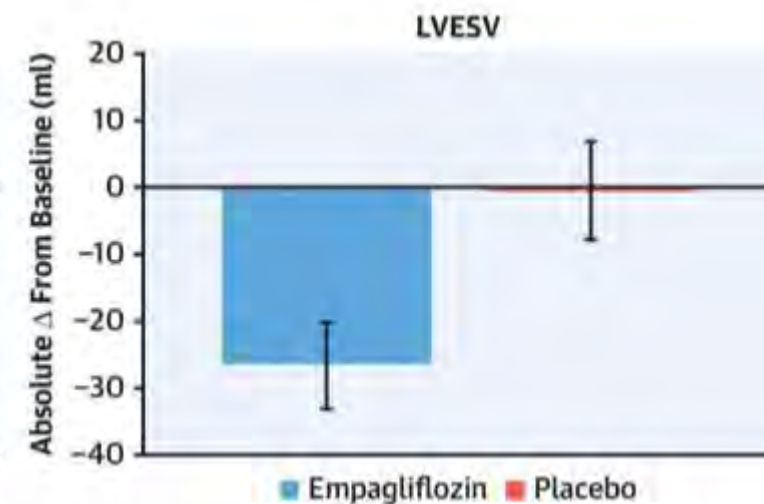
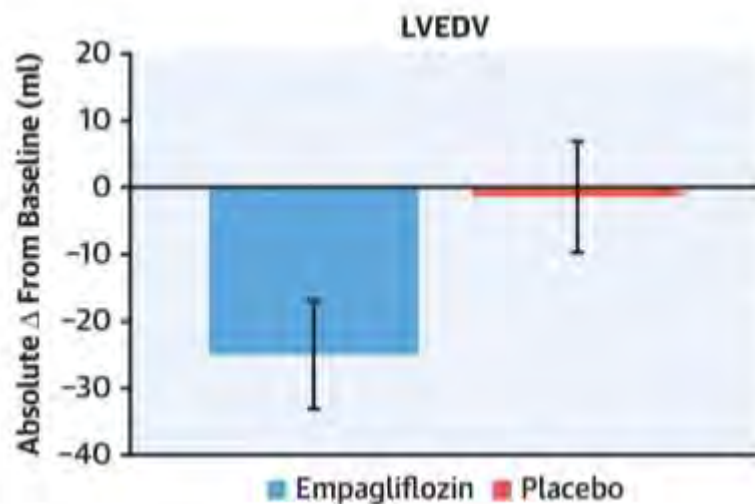
体脂肪低下
心外膜脂肪低下
血糖低下
血中尿酸低下
血中ケトン体増加
抗酸化作用



Randomized Trial of Empagliflozin in Nondiabetic Patients With Heart Failure and Reduced Ejection Fraction

Santos-Gallego, C.G. et al. J Am Coll Cardiol. 2021;77(3):243-55.

心臓の**組成**が
変わる



心外膜脂肪（EAT）と心不全

肥満や慢性炎症はEATの蓄積を促進。

間葉系幹細胞の遊走や形質転換および炎症性サイトカインの局所分泌を介した、**炎症**、**微小血管の粗造化**、**心筋線維化**がHFpEFの病態に関与。

Packer M : Epicardial Adipose Tissue May Mediate Deleterious Effects of Obesity and Inflammation on the Myocardium. J Am Coll Cardiol, 2018 ; 71 : 2360~ 2372

HFpEF患者では EATの量が多い

HFpEF に心房細動や 2型糖尿病合併は、 さらにEAT量が多い

van Woerden G1, et al.: Epicardial fat in heart failure patients with mid-range and preserved ejection fraction. Eur J Heart Fail, 2018 ; 20 : 1559~ 1566



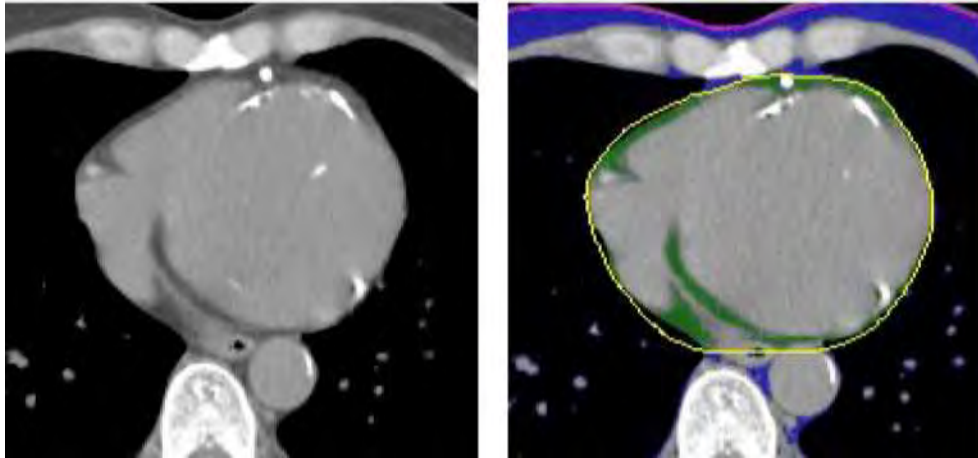
ORIGINAL INVESTIGATION

Open Access



The effect of dapagliflozin treatment on epicardial adipose tissue volume

Takao Sato¹, Yoshifusa Alzawa, Sho Yuasa, Shohei Kishi, Koichi Fuse, Satoru Fujita, Yoshio Ikeda, Hitoshi Kitazawa, Minoru Takahashi, Masahito Sato and Masaaki Okabe



SGLT2阻害薬
心外膜脂肪減
炎症反応改善

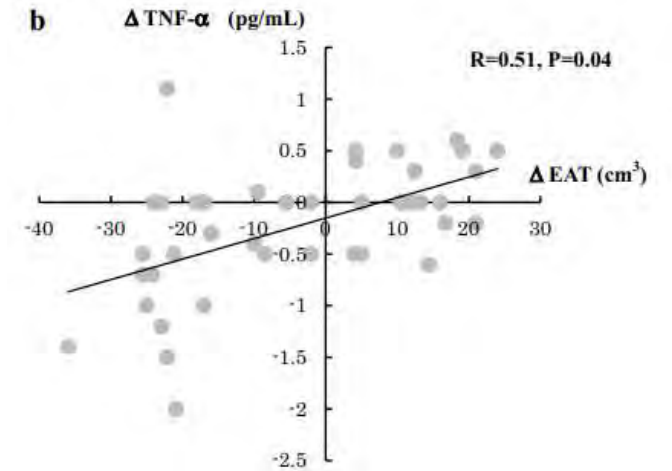
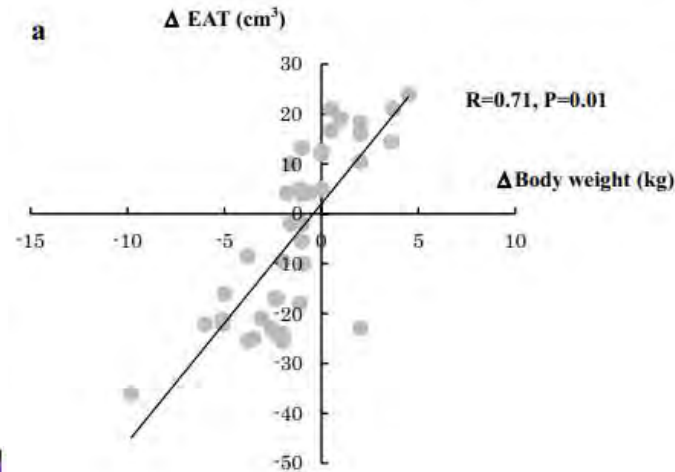


Table 5 Change rate of adipose-associated markers after treatment

	Dapagliflozin (n = 20)	Conventional therapy (n = 20)	p value, dapagliflozin vs. conventional
ΔEAT volume (cm ³)	-16.4 ± 8.3**	4.7 ± 8.8	0.01
ΔTNF-α (pg/ml)	-0.5 ± 0.7**	0.03 ± 0.3	0.03
ΔPAI-1 (ng/ml)	-10.1 ± 18.8*	-2.0 ± 9.7	0.18

EAT epicardial adipose tissue, TNF-α tumor necrosis factor-α, PAI-1 plasminogen activator inhibitor-1

Data are expressed as mean ± SD. ** p < 0.05 compared with baseline of each group, * p < 0.1 compared with baseline of each group



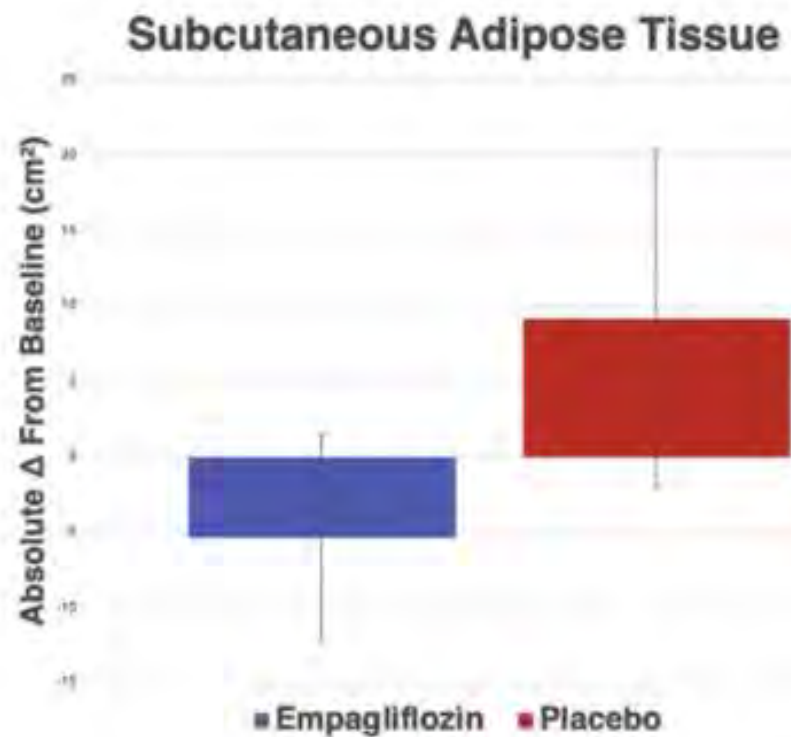
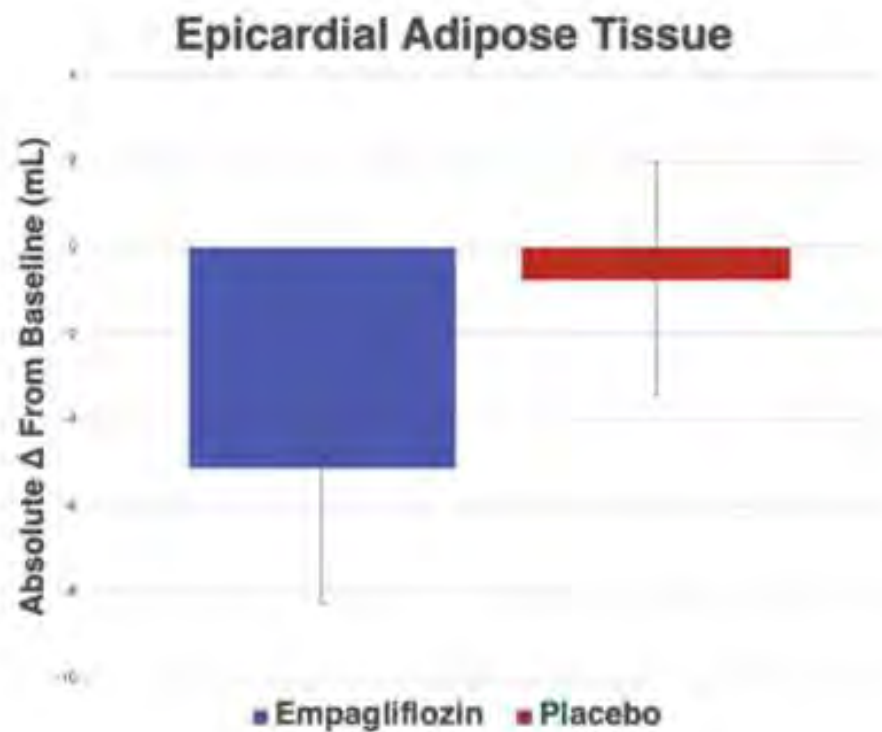
Mechanistic Insights of Empagliflozin in Nondiabetic Patients With HFrEF



From the EMPA-TROPISM Study

Juan Antonio Requena-Ibáñez, MD,^{a,b,*} Carlos G. Santos-Gallego, MD,^{a,b,*} Anderly Rodriguez-Cordero, MD,^{a,b} Ariana P. Vargas-Delgado, MD,^{a,b} Donna Mancini, MD,^b Samantha Sartori, PhD,^b Farah Atallah-Lajam, MD,^b Chiara Giannarelli, MD, PhD,^b Frank Macaluso, BSc,^b Anuradha Lala, MD,^b Javier Sanz, MD,^b Valentin Fuster, MD, PhD,^b Juan José Badimon, PhD^{a,b}

HFrEF非糖尿病患者において
脂肪量を有意に改善



Mechanistic Insights of Empagliflozin in Nondiabetic Patients With HFrEF

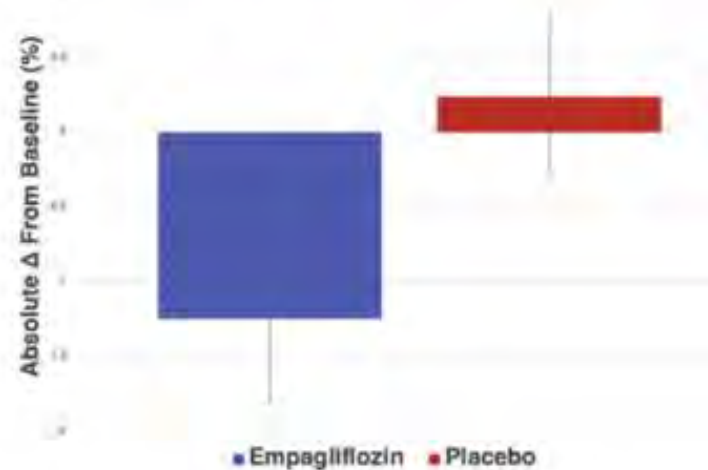


From the EMPA-TROPISM Study

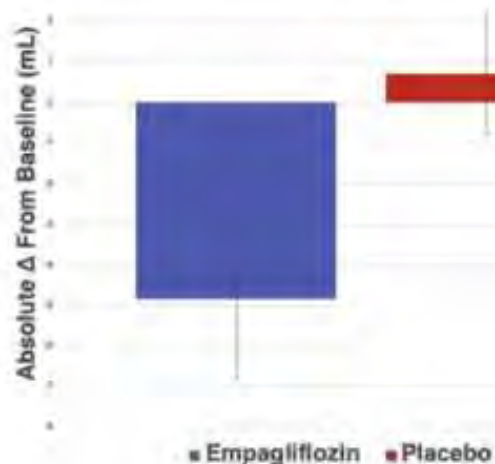
Juan Antonio Requena-Ibáñez, MD,^{a,b,*} Carlos G. Santos-Gallego, MD,^{a,b,*} Anderly Rodriguez-Cordero, MD,^{a,b}
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Valentin Fuster, MD, PhD,^b Juan José Badimon, PhD^{a,b}

HFrEF非糖尿病患者において
心筋肥大、間質、心筋線維を
有意に改善

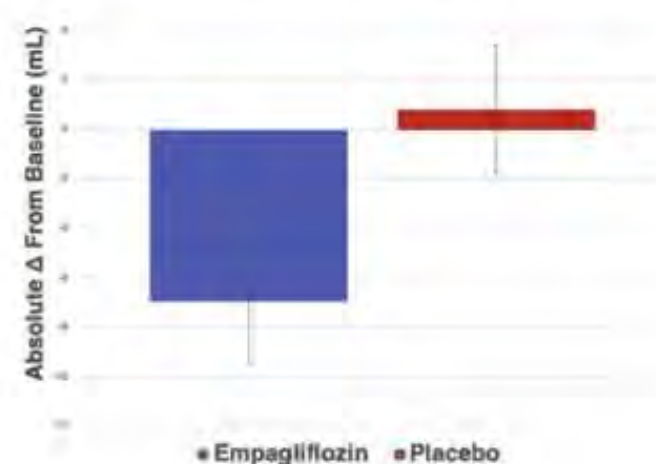
A Extracellular volume



B Matrix Volume



C Cardiomyocyte volume



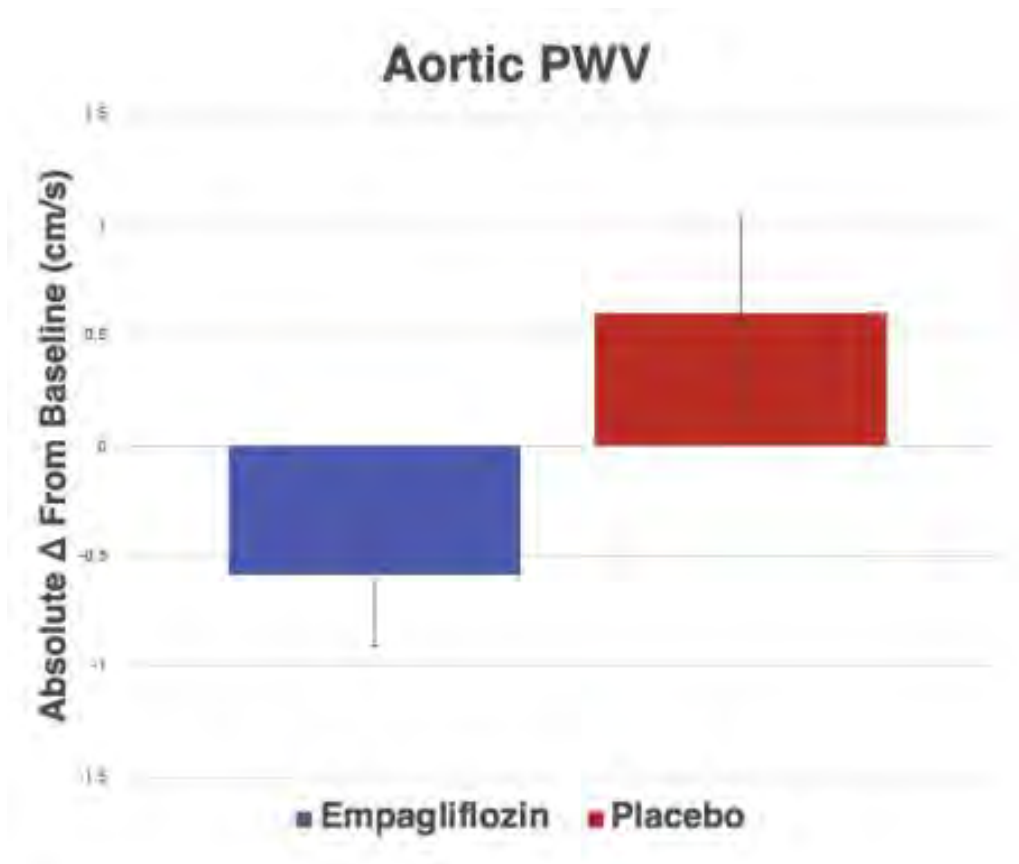
Mechanistic Insights of Empagliflozin in Nondiabetic Patients With HFrEF



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Juan Antonio Requena-Ibáñez, MD,^{a,b,*} Carlos G. Santos-Gallego, MD,^{a,b,*} Anderly Rodriguez-Cordero, MD,^{a,b} Ariana P. Vargas-Delgado, MD,^{a,b} Donna Mancini, MD,^b Samantha Sartori, PhD,^b Farah Atallah-Lajam, MD,^b Chiara Giannarelli, MD, PhD,^b Frank Macaluso, BSc,^b Anuradha Lala, MD,^b Javier Sanz, MD,^b Valentin Fuster, MD, PhD,^b Juan José Badimon, PhD^{a,b}

HFrEF非糖尿病患者において
大動脈硬化、炎症マーカーを
有意に改善





Review

A new class of drugs for heart failure: SGLT2 inhibitors reduce sympathetic overactivity

Motoaki Sano (MD, PhD, FJCC)*

Department of Cardiology, Keio University School of Medicine, Tokyo, Japan



SGLT2阻害薬は 交感神経を抑制

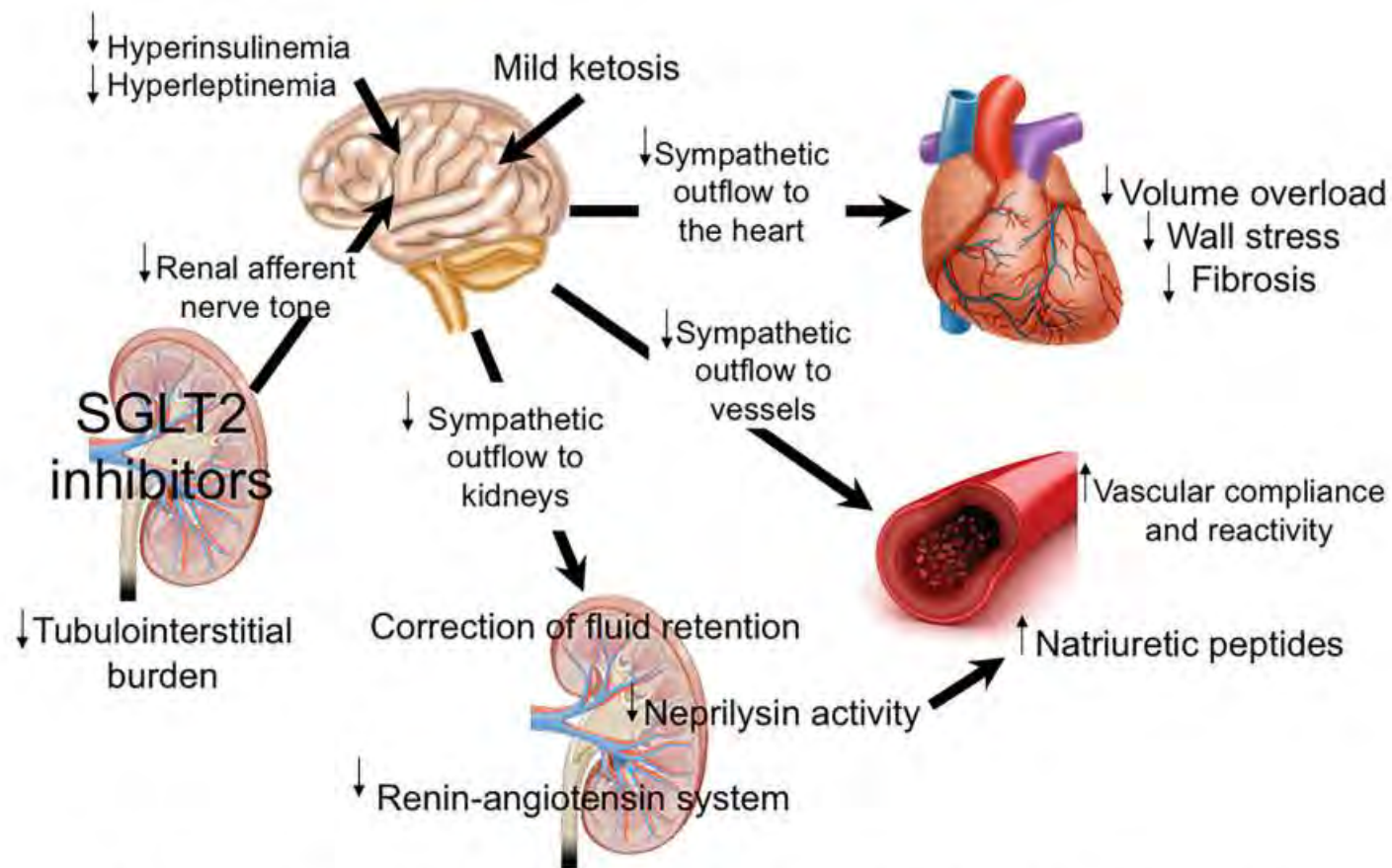


Fig. 1. Proposed mechanism of cardiovascular protection by SGLT2 inhibitors. SGLT2, sodium glucose cotransporter 2.

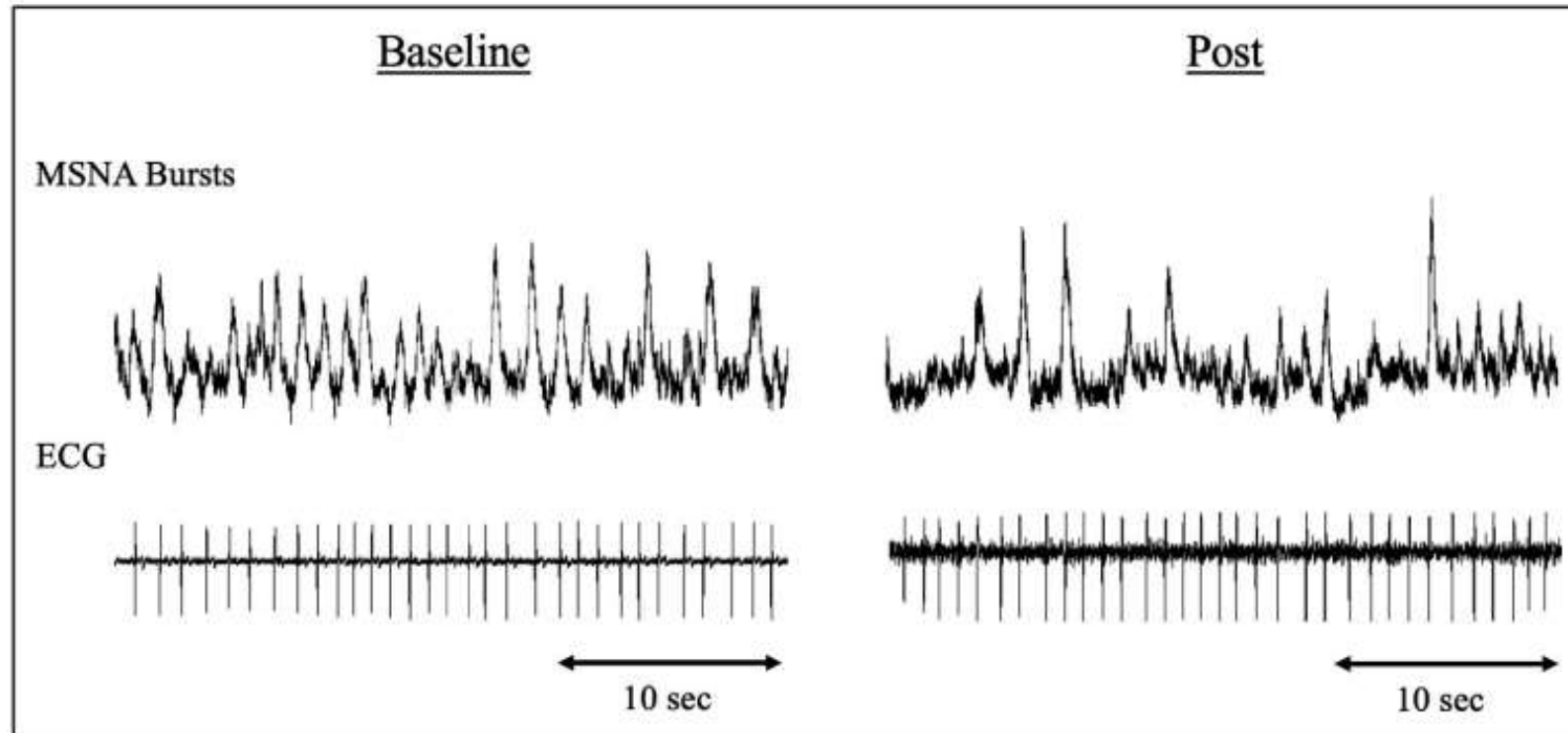


ORIGINAL RESEARCH

Different Responses of Muscle Sympathetic Nerve Activity to Dapagliflozin Between Patients With Type 2 Diabetes With and Without Heart Failure

Takuto Hamaoka, MD, PhD; Hisayoshi Murali, MD, PhD; Tadayuki Hirai, MD; Hiroyuki Sugimoto, MD; Yusuke Mukai, MD; Oto Inoue, MD, PhD; Shinichiro Takashima, MD, PhD; Takeshi Kato, MD, PhD; Shigeo Takata, MD, PhD; Soichiro Usui, MD, PhD; Kenji Sakata, MD, PhD; Masa-Aki Kawashiri, MD, PhD; Masayuki Takamura, MD, PhD

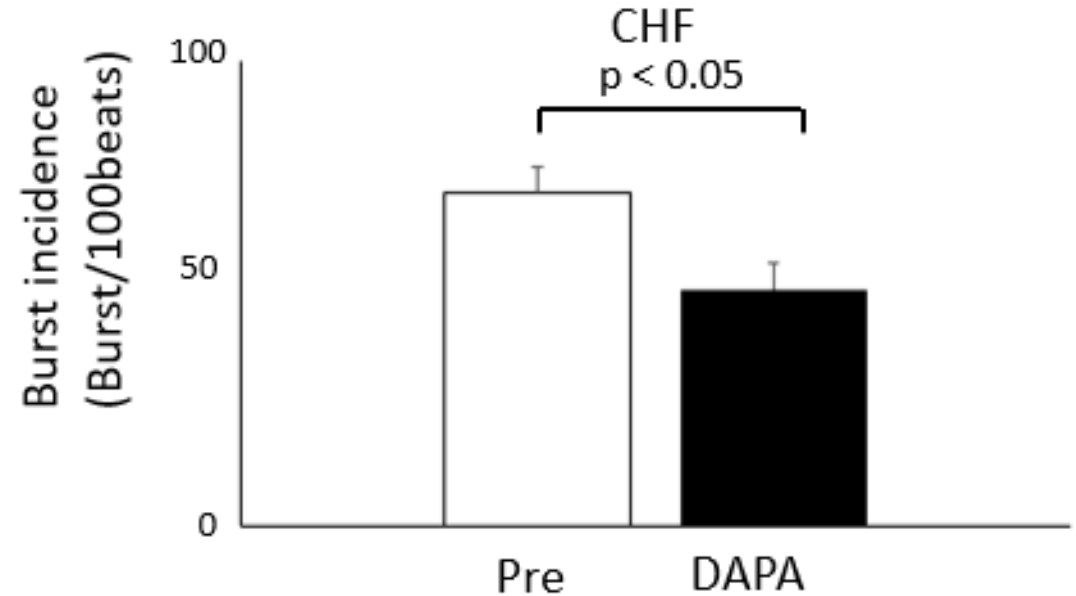
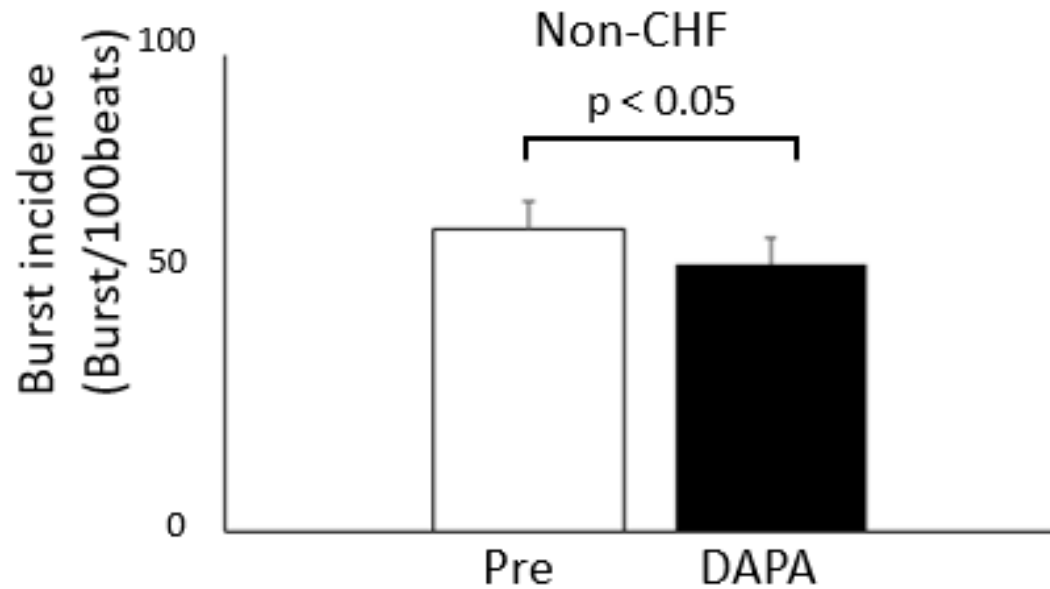
Dapagliflozin 投与12週間後 筋交感神経活動 (MSNA) 減



ORIGINAL RESEARCH

Different Responses of Muscle Sympathetic Nerve Activity to Dapagliflozin Between Patients With Type 2 Diabetes With and Without Heart Failure

Takuto Hamaoka, MD, PhD; Hisayoshi Murali, MD, PhD; Tadayuki Hirai, MD; Hiroyuki Sugimoto, MD; Yusuke Mukai, MD; Oto Inoue, MD, PhD; Shinichiro Takashima, MD, PhD; Takeshi Kato, MD, PhD; Shigeo Takata, MD, PhD; Soichiro Usui, MD, PhD; Kenji Sakata, MD, PhD; Masa-Aki Kawashiri, MD, PhD; Masayuki Takamura, MD, PhD



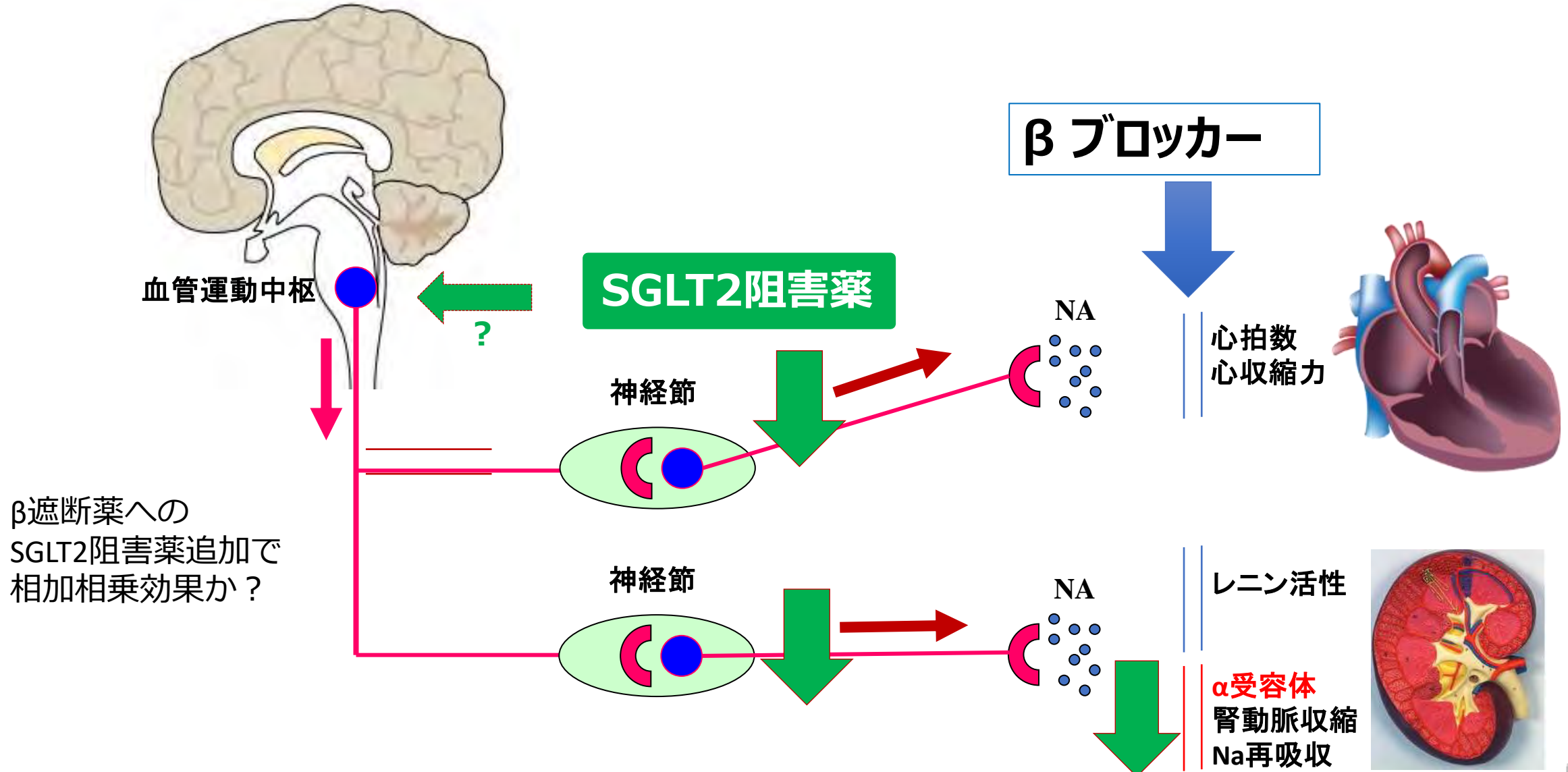
Dapagliflozin 投与12週間後 CHFの有無に関わらず 筋交感神経活動（MSNA）減

β遮断薬ではMSNAは変化しない

金沢市立病院村井久純先生提供 論文から作図



SGLT2阻害薬の交感神経活動に対する効果



中枢に対する抑制の3つの可能性（仮説）

2つの間接的経路と1つの直接経路が想定

- ①腎臓の交感神経刺激の求心路を抑制、中枢の血管運動中枢を下げる
- ②頸動脈圧受容体の感受性を亢進→迷走神経の求心路亢進→中枢改善
- ③脂溶性が高く血液脳関門を通り、直接血管運動中枢抑制

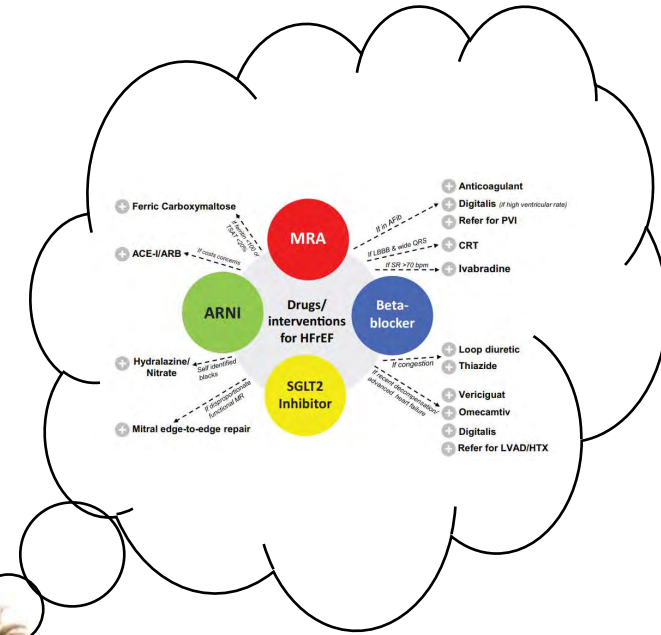


ポリファーマシーと投与順番

ポリファーマシー



投与順番



2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure

A Report of the American College of Cardiology/American Heart Association
Joint Committee on Clinical Practice Guidelines

COR	LOE	RECOMMENDATION
1	A	1. In patients with symptomatic chronic HFrEF, SGLT2i are recommended to reduce hospitalization for HF and cardiovascular mortality, irrespective of the presence of type 2 diabetes (1,2).
2a	B-R	2. In patients with HFpEF, SGLT2i can be beneficial in decreasing HF hospitalizations and cardiovascular mortality (4).



OPEN

Polypharmacy and Clinical Outcomes in Hospitalized Patients With Acute Decompensated Heart Failure

Neiko Ozasa, MD, PhD; Takao Kato, MD, PhD; Takeshi Morimoto, MD, MPH; Hidenori Yaku, MD, PhD; Erika Yamamoto, MD, PhD; Yasutaka Inuzuka, MD, PhD; Yodo Tamaki, MD, PhD; Takeshi Kitai, MD, PhD; Koichi Washida, MSN; Yuta Seko, MD; Yusuke Yoshikawa, MD; Yukihiro Sato, MD, PhD; Hirohiko Motoki, MD, PhD; Koichiro Kuwahara, MD, PhD; Takeshi Kimura, MD, PhD

Fantastic 4
たかが4剤？ or 4剤も？



■ Q1 ■ Q2 ■ Q3 ■ Q4

中央値 8 最大24

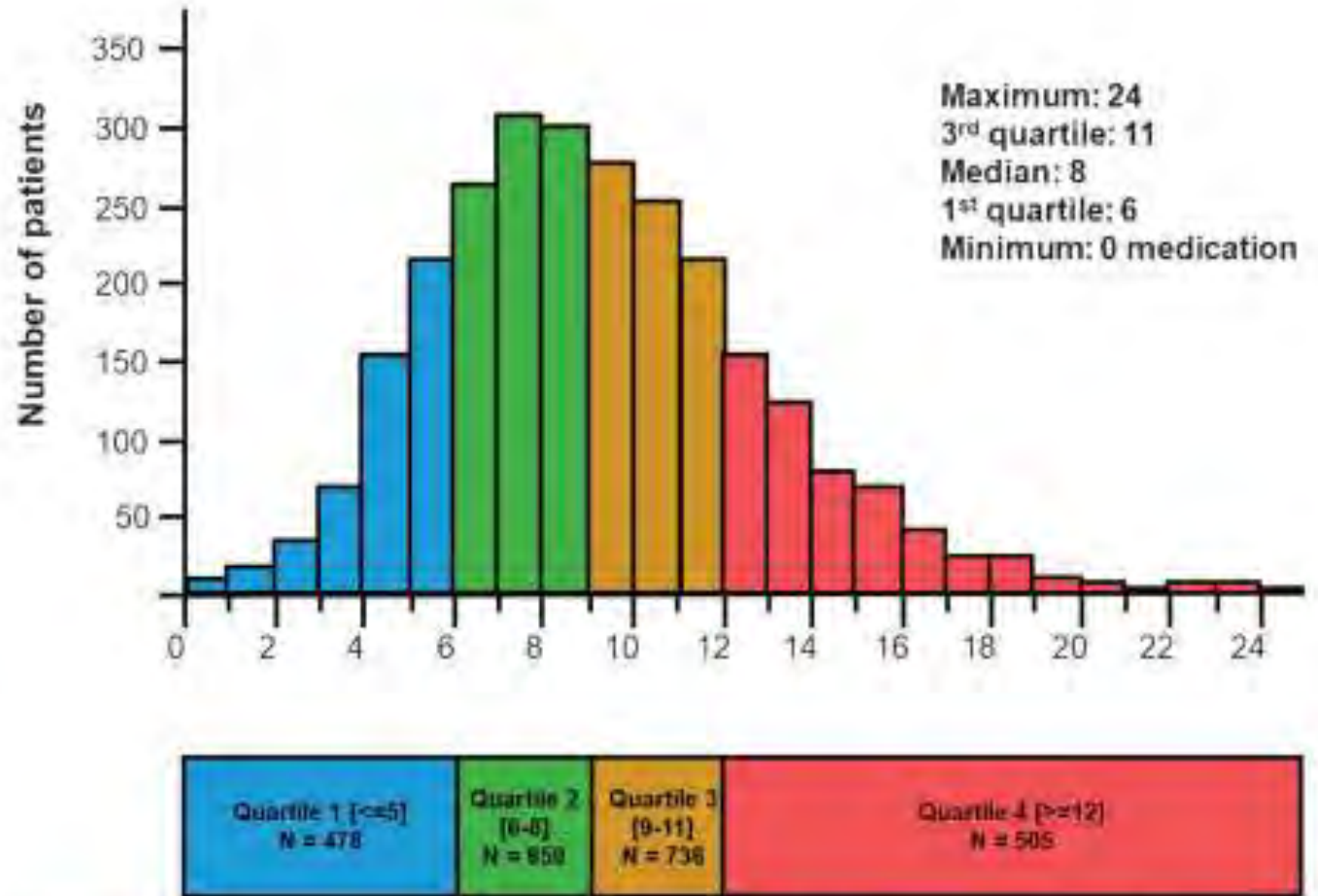


FIGURE 2. Number of medications at discharge from the index hospitalization.



Heart failure: how to optimize guideline-directed medical therapy

Filippo Crea^{1,2}

¹University of Campania "Filippo Stabia" Public University, A. Cardillo (RCA) Policlinic, Naples, ²Department of Cardiovascular and Pulmonary Medicine, Cornell University, in the United States, Rome, Italy

With thanks to Anika Meier-Betschler, Johanna Huggler, and Martin Meyer for help with completion of this article.



SGLT2iを
最も最初に
導入がよい



SGLT2i
MRA
β-blocker
ARNI

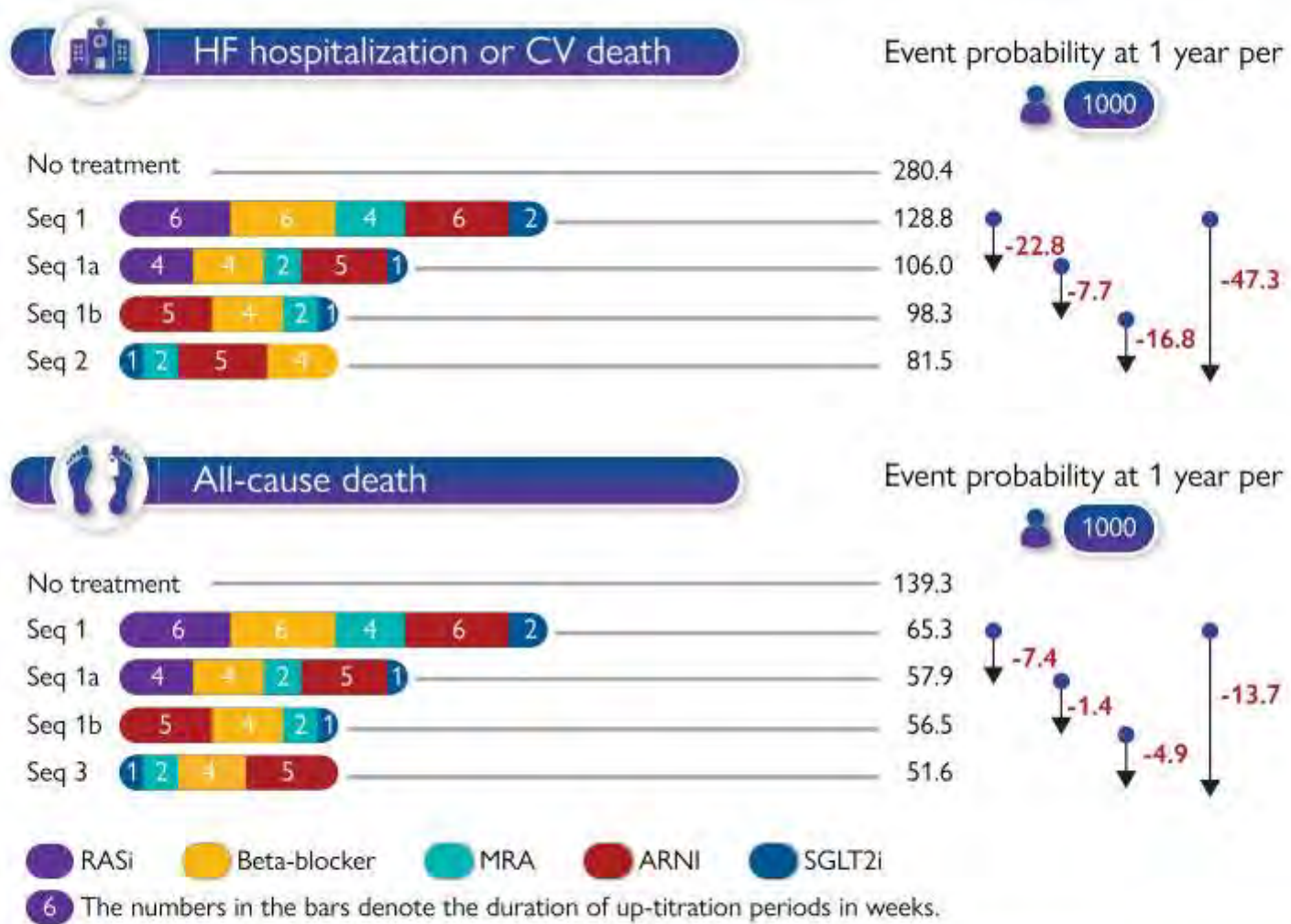


Figure 2 Potential reductions in events from accelerated up-titration and optimized ordering of treatment sequence compared with the conventional schedule.¹⁷



Accelerated and personalized therapy for heart failure with reduced ejection fraction

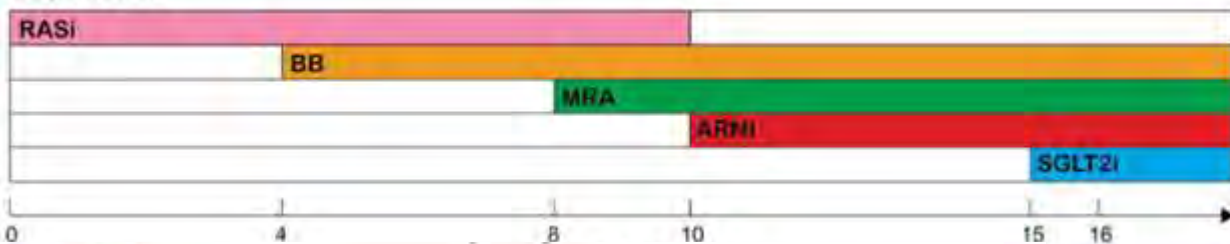
Li Shen^{1,2}, Pardeep Singh Jhund², Kieran Francis Docherty¹, Muthiah Vaduganathan¹, Mark Colquhoun Petrie^{3,4}, Akshay Suvas Desai¹, Lars Køber⁵, Morten Schou⁵, Milton Packer^{6,7}, Scott David Solomon¹, Xingwei Zhang¹, and John Joseph Valentine McMurray^{1,2*}

*Correspondence: J. J. V. McMurray, ESC Heart Failure Unit, University of Glasgow, 100 West George Street, Glasgow G4 7TA, UK. Email: j.j.v.mcmurray@glasgow.ac.uk

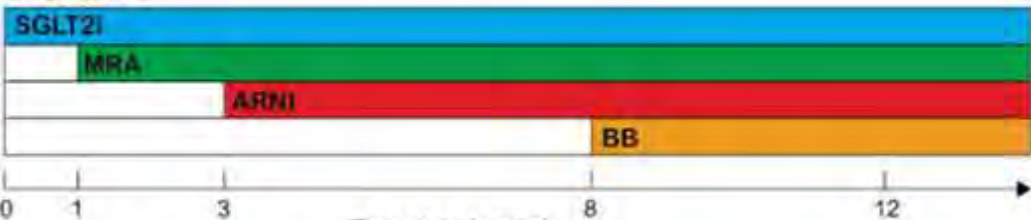
Sequence 1



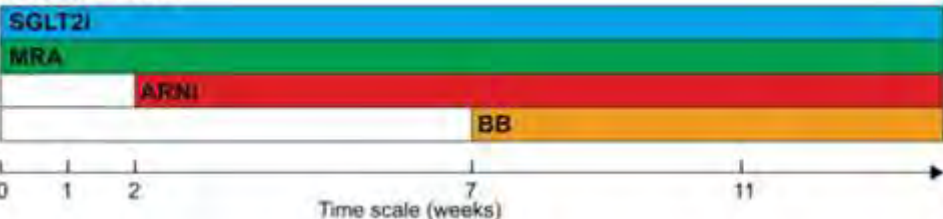
Sequence 1a



Sequence 2



Sequence duo 2



より**早期**にSGLT2i導入
 より**早期**に重ねていく

1年間の心不全入院+心血管死

280/1000(未治療)

129/1000

108/1000

82/1000

77/1000

SGLT2阻害薬とMRA同時投与
 → + ARNI → + β遮断薬



Redefining β -blocker response in heart failure patients with sinus rhythm and atrial fibrillation: a machine learning cluster analysis



Andreas Karwath, Karina V Bunting, Simrat K Gill, Otilia Tica, Samantha Pendleton, Furqan Aziz, Andrey D Barsky, Saisakul Chernbumroong, Jinming Duan, Alastair R Mobley, Victor Roth Cardoso, Luke Slater, John A Williams, Emma-Jane Bruce, Xiaoxia Wang, Marcus D Flather, Andrew J S Coats, Georgios V Gkoutos, Dipak Kotecha, on behalf of the cardAIC group and the Beta-blockers in Heart Failure Collaborative Group*



β blockers in cluster AF2, with an adjusted OR of 0.57 (95% CI 0.35–0.93; $p=0.023$) and NNT of 17.4. This cluster ($n=659$) was comprised of younger patients with lower rates of previous myocardial infarction

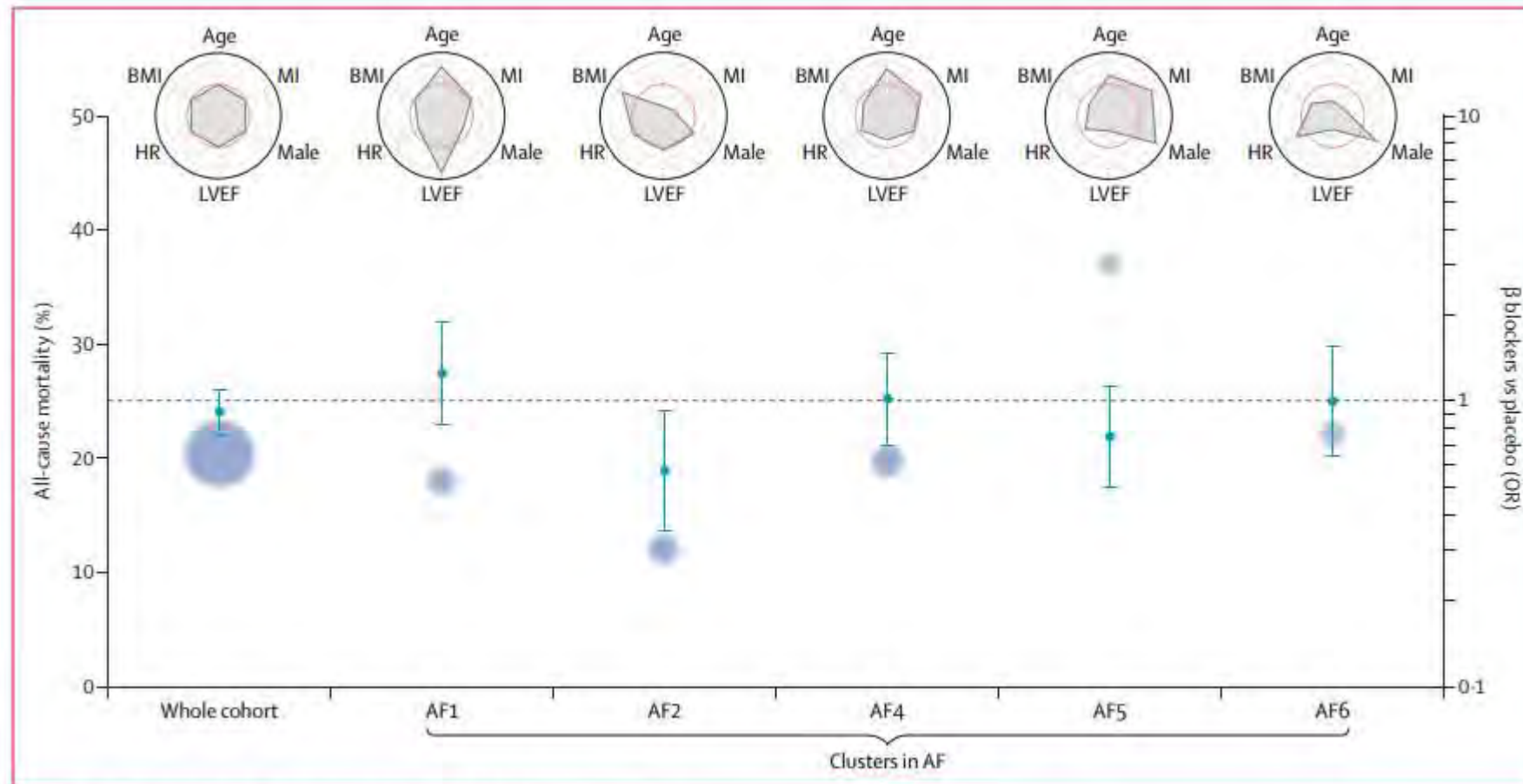


Figure 3: Clustering for all-cause mortality and β -blocker efficacy in AF

Cost-effectiveness of dapagliflozin as a treatment for heart failure with reduced ejection fraction: a multinational health-economic analysis of DAPA-HF

Phil McEwan^{1*}, Oliver Darlington¹, John J.V. McMurray², Pardeep S. Jhund², Kieran F. Docherty³, Michael Böhm³, Mark C. Petrie³, Klas Bergenheim⁴, and Lei Qin⁵

費用対効果

SGLT 2 i追加

標準治療

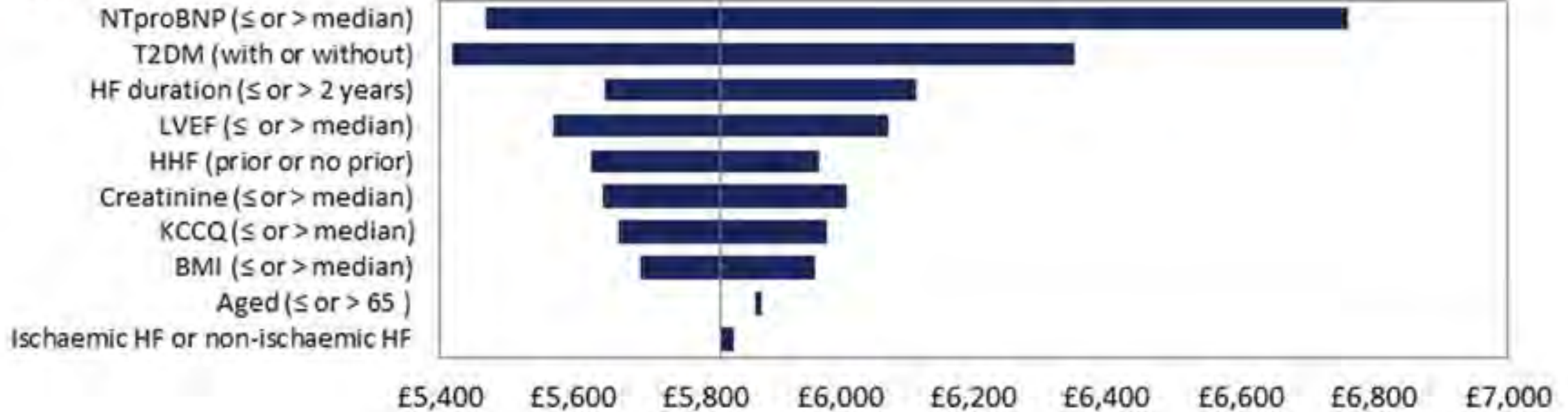
	Dapagliflozin + standard therapy		Standard therapy	Incremental
UK				
Total costs	£16 408		£13 628	£2780
Treatment, monitoring and adverse events	£4287		£1917	£2370
Worsening HF events and CV death	£3851	薬剤費 > 追加治療費	£4229	- £378
Background resource use	£8270	QALYは改善	£7482	£788
Total LYs	6.20		5.62	0.58
Total QALYs	4.61		4.13	0.48
ICER	-		-	£5822/QALY
Clinical events^a				
HHF (per 1000 treated patients)	820		925	-105
Urgent HF visit (per 1000 treated patients)	32		54	-22
1-year survival	91.8%	心不全	90.3%	1.6%
2-year survival	82.7%	緊急受診	79.6%	3.1%
5-year survival	56.6%	生存率の改善	50.9%	5.7%

Cost-effectiveness of dapagliflozin as a treatment for heart failure with reduced ejection fraction: a multinational health-economic analysis of DAPA-HF

Phil McEwan^{1*}, Oliver Darlington¹, John J.V. McMurray², Pardeep S. Jhund², Kieran F. Docherty², Michael Böhm³, Mark C. Petrie², Klas Bergenheim⁴, and Lei Qin⁵

一般的に許容されるのは £ 20,000/ 1 QALY

United Kingdom



この研究はAstraZenecaのサポートあり

Cost-effectiveness of dapagliflozin as a treatment for heart failure with reduced ejection fraction: a multinational health-economic analysis of DAPA-HF

Phil McEwan^{1*}, Oliver Darlington¹, John J.V. McMurray², Pardeep S. Jhund², Kieran F. Docherty², Michael Böhm³, Mark C. Petrie², Klas Bergenheim⁴, and Lei Qin¹

ARNIとの費用対効果比較

	ARNI	SGLT2i
Risk Reduction	20	26
QALY gains	0.42	0.48
Cost/1 QALY	17,100	5,822

McMurray JJ, et al. Cost-effectiveness of sacubitril/valsartan in the treatment of heart failure with reduced ejection fraction. Heart 2018;104:1006–1013.

まっさきに選ぶ





やわたメディカルセンター
YAWATA MEDICAL CENTER
病気にならないための病院





ガイドラインの薬さえ
出してあげばいいだろ



演者の個人的見解





心リハ





Heart Failure: An Underappreciated Complication of Diabetes. A Consensus Report of the American Diabetes Association

Diabetes Care 2022;45:1670-1690 | <https://doi.org/10.2337/dci22-0014>



Radica Pop-Busui,¹ James L. Januzzi,² Dennis Bruemmer,³ Sonia Butala,⁴ Jennifer B. Green,⁵ William B. Harton,⁶ Colette Knight,⁷ Moshe Levi,⁸ Neda Rasouli,⁹ and Caroline R. Richardson¹⁰

Special Considerations **Cardiac Rehabilitation** Diabetes Careに掲載

Cardiac rehabilitation programs are **underutilized** for those with diabetes and HFrEF.

Participation in cardiac rehabilitation is associated with improvement in exercise capacity and health status and possibly reduces mortality.

Efforts to increase **routine referral** of eligible individuals to cardiac rehabilitation are encouraged.



CQ3 保存期 CKD 患者に運動療法は推奨されるか？

【推奨文】

保存期 CKD 患者に対し、年齢や身体機能を考慮しながら可能な範囲で運動療法を行うことを提案する。【2C】

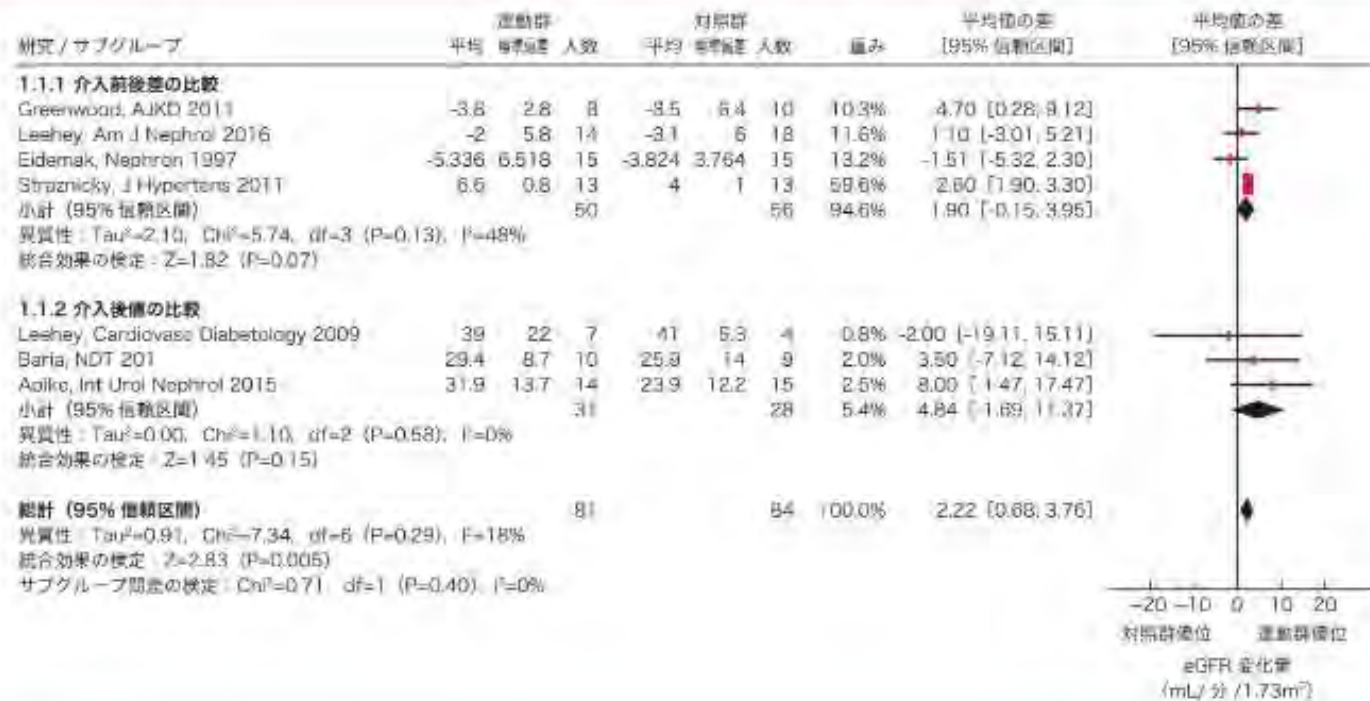
eGFR 変化量の記載がある 7 論文メタアナリシス
 12~24 週の運動介入により eGFR は有意に増加
 (+2.22[0.68~3.76]mL/分/1.73m²(I²=18%))

GUIDELINE FOR
 RENAL REHABILITATION

腎臓リハビリテーション ガイドライン

日本腎臓リハビリテーション学会

南正樹



ORIGINAL ARTICLE

Multidisciplinary Cardiac Rehabilitation and Long-Term Prognosis in Patients With Heart Failure

Kentaro Kamiya, PT, PhD; Yukihiko Saito, MD, PhD; Tetsuya Takatsuki, PT, PhD; Miyuki Tsuchihashi-Matsuyama, RN, PhD; Norihiko Kotooka, MD, PhD; Toyomi Wagahe, RN, MSN; Tomiyuki Takata, PhD; Takamitsu Yamamoto, MD, PhD; Makoto Nagayama, MD, PhD; Yoichi Goto, MD, PhD; Shigeru Makita, MD, PhD; Mitsuru Isobe, MD, PhD

日本人心不全への心リハ介入は全死亡、心不全再入院を減らす

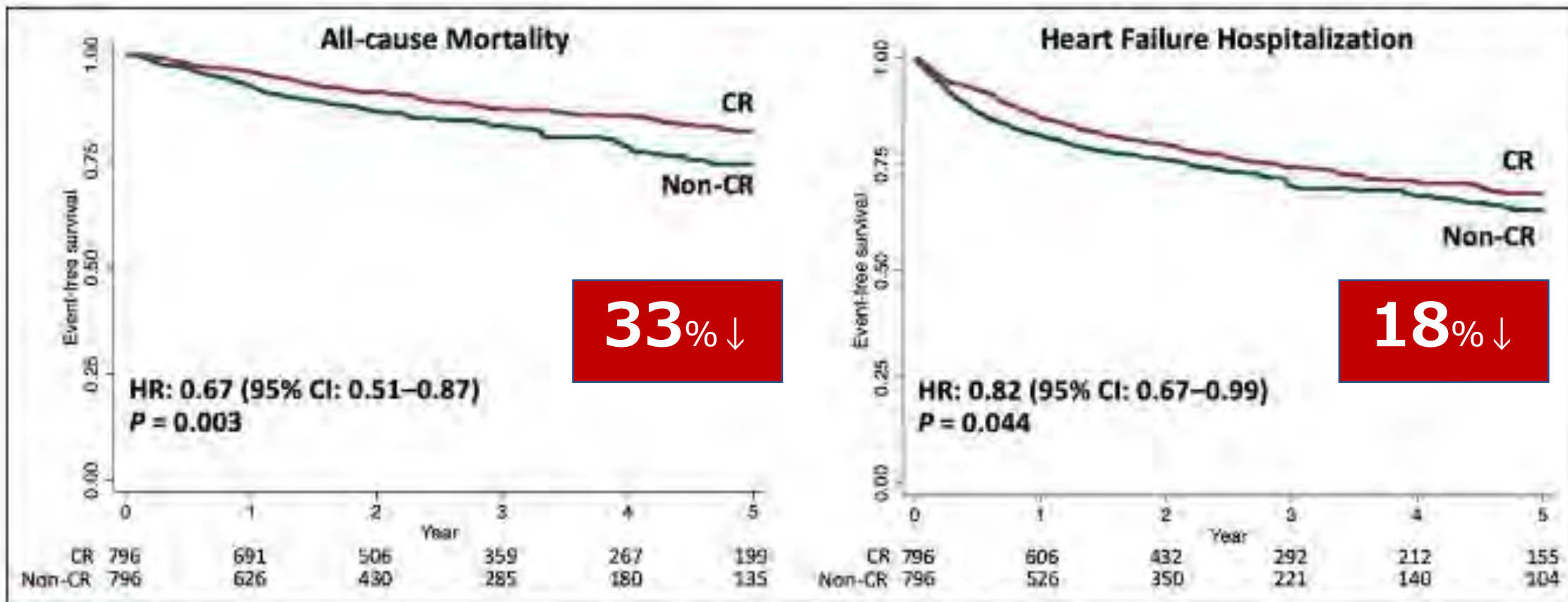


Figure 3. Cardiac rehabilitation (CR) and all-cause mortality or heart failure hospitalization. HR indicates hazard ratio.



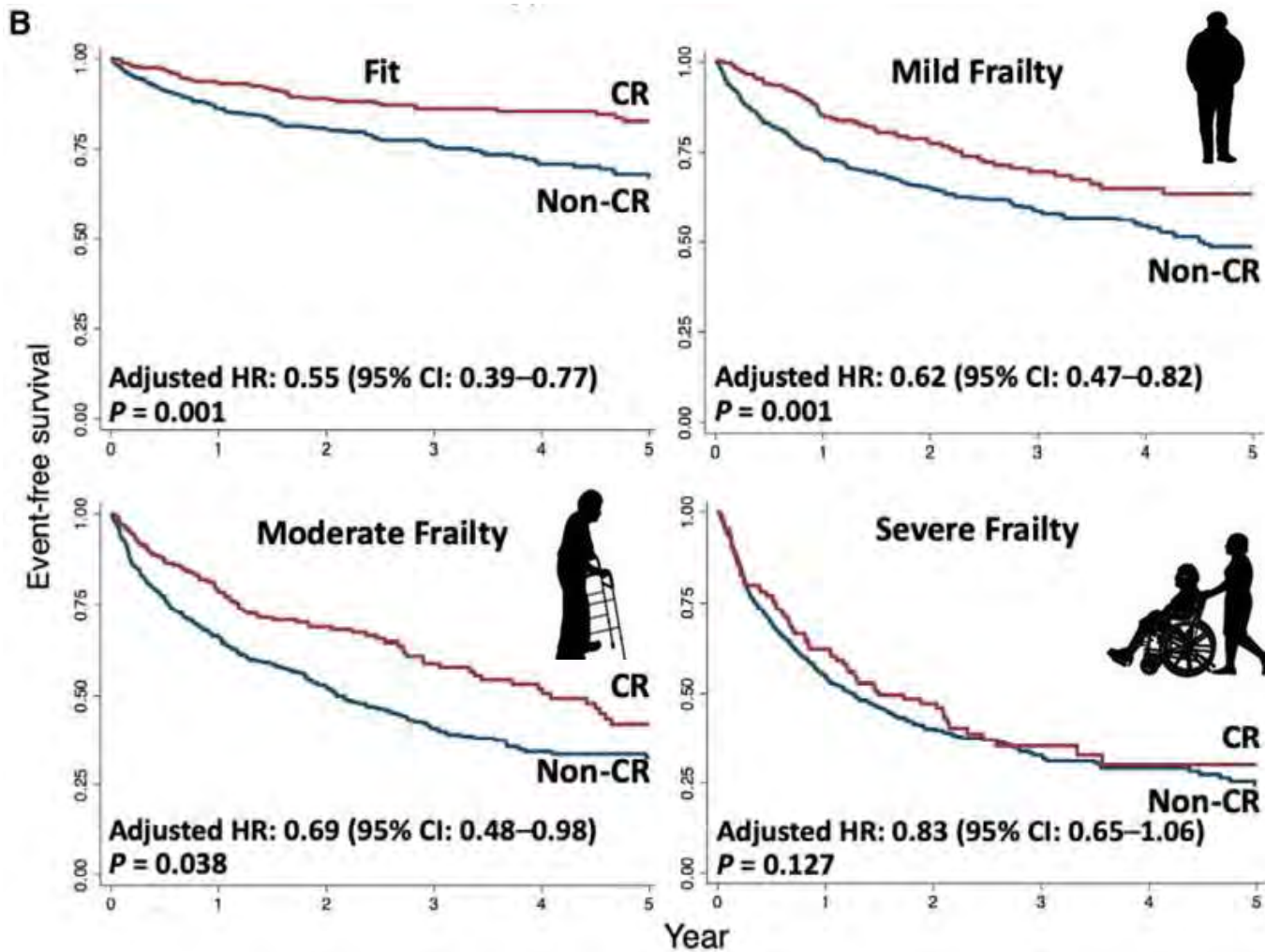
ORIGINAL ARTICLE

Multidisciplinary Cardiac Rehabilitation and Long-Term Prognosis in Patients With Heart Failure

Kentaro Kamiya¹, PT, PhD; Yukihiko Sato, MD, PhD; Tetsuya Takahashi, PT, PhD; Miyuki Tsuchinashi-Makawa, RN, PhD; Rionhisa Katooka², MD, PhD; Tetsuya Wajima, RN, MSN; Tetsuyuki Takahashi, PhD; Takamitsu Yamamoto³, MD, PhD; Masatoshi Nagayama, MD, PhD; Yoichi Goto⁴, MD, PhD; Shigenori Makita, MD, PhD; Mitsunori Isobe⁵, MD, PhD

フレイル合併例への心リハは有効

Kamiya K et al. Circ Heart Fail 2020



Family Caregiving for Individuals With Heart Failure: A Scientific Statement From the American Heart Association

Knowledge Support	Support with Care Tasks
<ul style="list-style-type: none">Understanding prognosisAssessing what to expect and how to care for patients at end-of-lifeUnderstanding palliative care and end-of-life options	<ul style="list-style-type: none">Managing common symptomsManaging medication, changing medicationsManaging complex medical devicesWorking in a caregiver role can be stressful
Support Navigating Health Systems	Support with Personal/Family Issues
<ul style="list-style-type: none">Care coordination (e.g., between providers)Navigating insurance and coverageHandling billing issuesAppropriately accessing health services and supports	<ul style="list-style-type: none">Addressing spiritual and bereavement needsAddressing financial issuesAddressing caregiver health and well-beingCoping with uncertainty, fearManaging difficult conversationsSeeking for help from community

介護者支援の視点も必要

介護の持続可能性を語る

Figure 2. Standardized needs of caregivers of patients with advanced heart failure as they approach the end of life.¹⁴

ORIGINAL ARTICLE

Multidisciplinary Cardiac Rehabilitation and Long-Term Prognosis in Patients With Heart Failure

Kentaro Kamiya¹, PT, PhD; Yukihiko Saito, MD, PhD; Tetsuya Takatsuki, PT, PhD; Miyuki Tsuchinashi-Makawa, RN, PhD; Rionhiko Katooka², MD, PhD; Tetsuya Nagano, RN, MSN; Tetsuyuki Takahara, PhD; Takahiro Yamamoto, MD, PhD; Masatoshi Nagayama, MD, PhD; Yoichi Goto³, MD, PhD; Shigenori Makita, MD, PhD; Mitsuki Isobe⁴, MD, PhD

HFrEFのみならずHFpEFにも効く

Kamiya K et al. Circ Heart Fail 2020

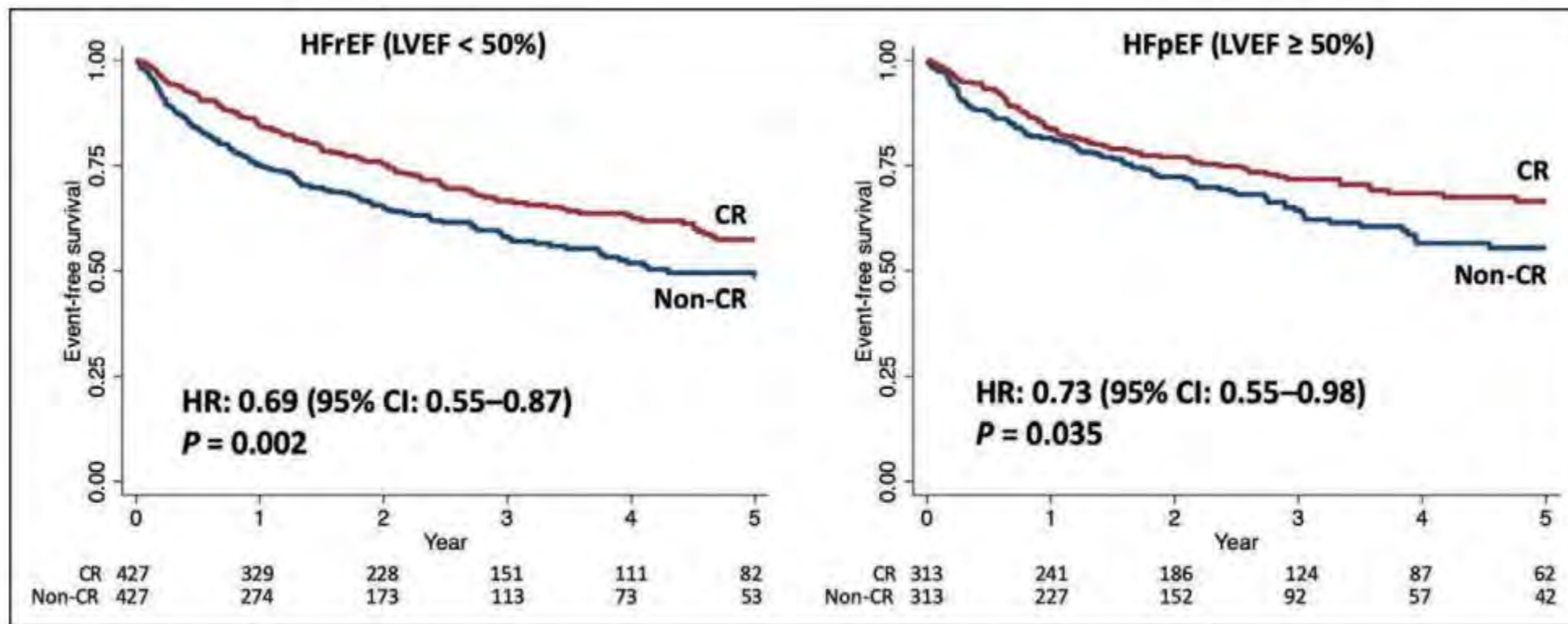


Figure 6. Cardiac rehabilitation (CR) and outcomes across left ventricular ejection fraction (LVEF) categories.

HFpEF indicates heart failure with preserved ejection fraction; HFrEF, heart failure with reduced left ventricular ejection fraction; and HR, hazard ratio.



Rehabilitation Intervention in Older Patients With Acute Heart Failure With Preserved Versus Reduced Ejection Fraction

HFrEFよりHFpEFの方が心リハの効果量が大き

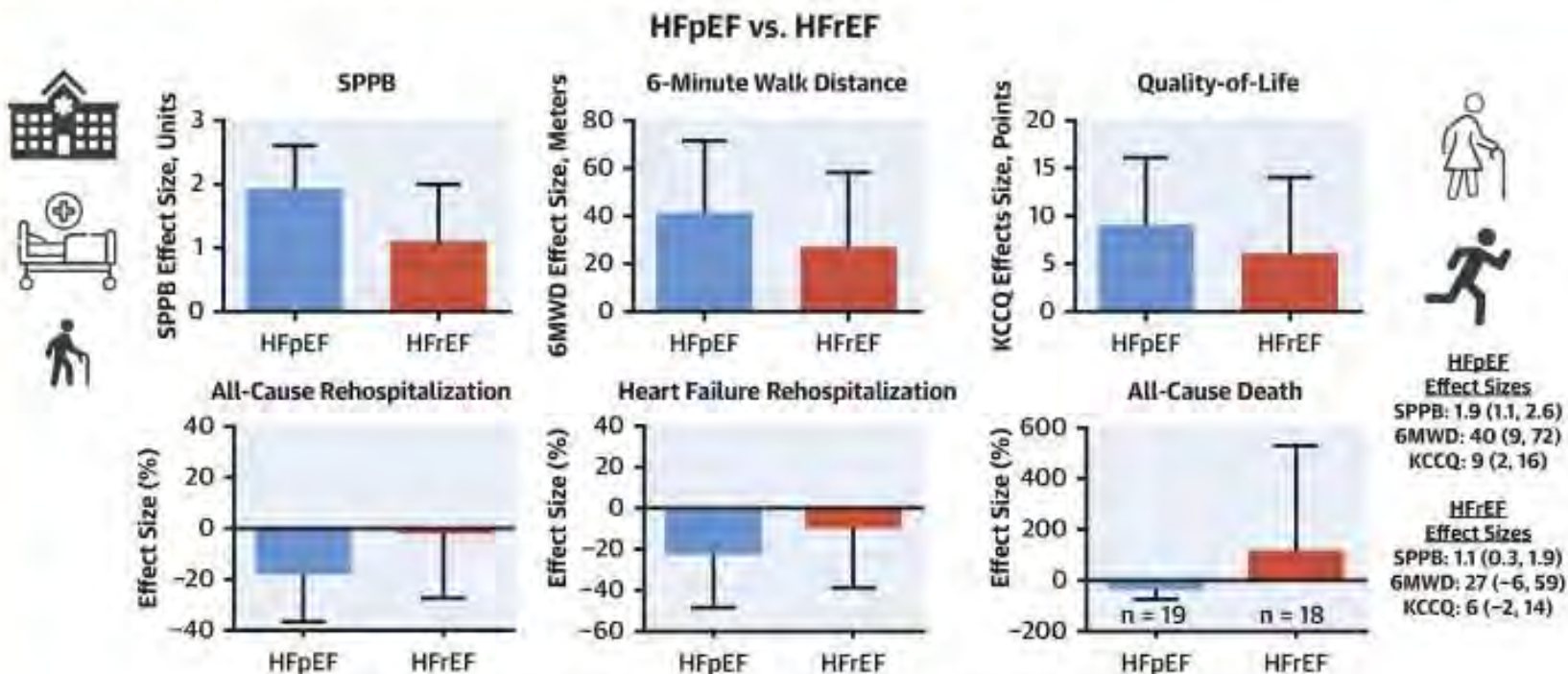
HFpEF患者
女性が多く (HFpEF :
61%、HFrEF : 43%)

ベースラインの身体機能、
フレイル、QOL、抑うつ
有意に不良



SPPBのスコア
HFrEF患者 + 1.1
HFpEF患者 + 1.9で大
6 MD, QOLも
HFpEFが効果大

CENTRAL ILLUSTRATION: Novel Rehabilitation Intervention in Older Patients With Acute Decompensated Heart Failure



Compared to patients with HFrEF, those with HFpEF may derive greater benefit from the intervention.

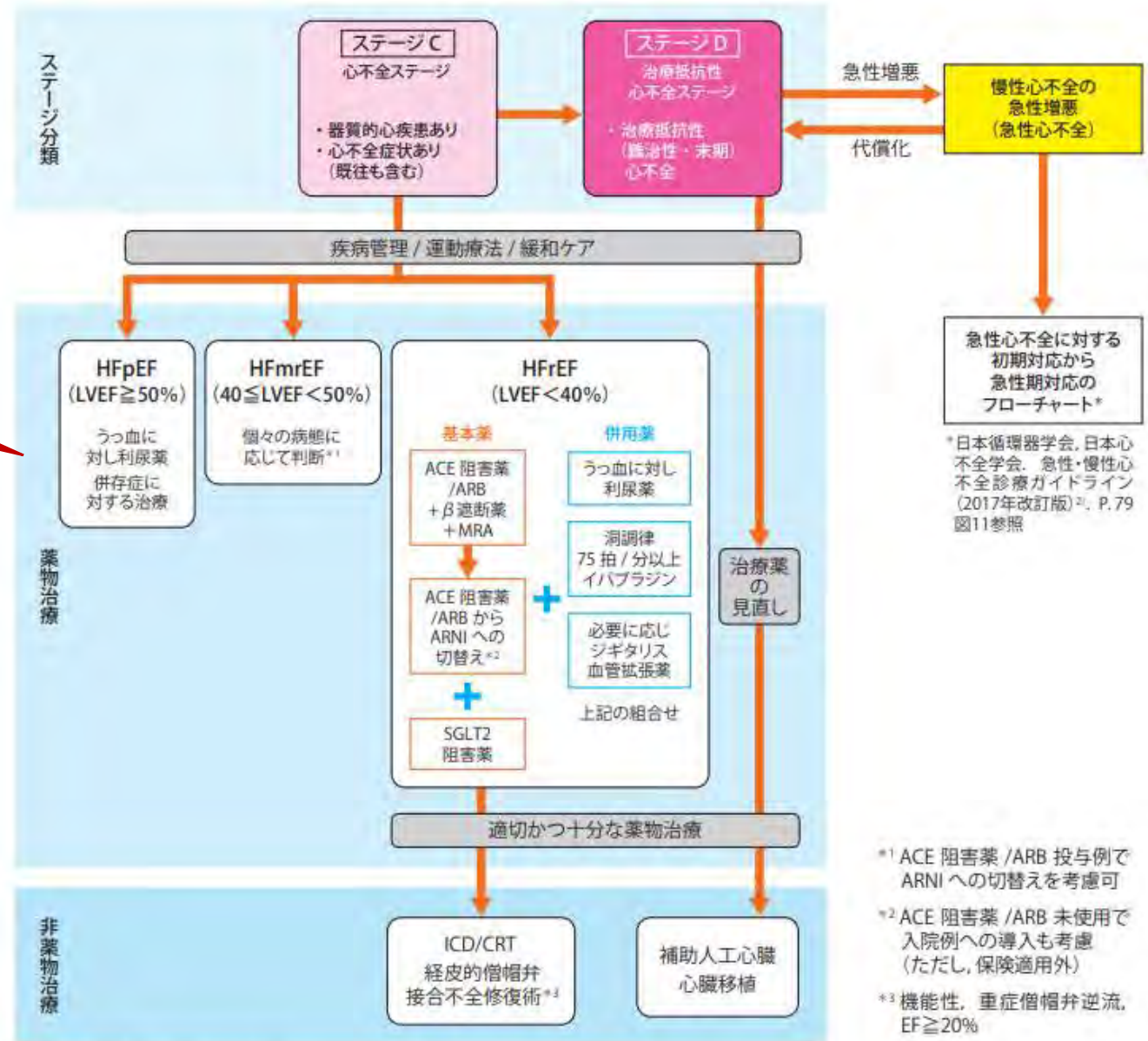
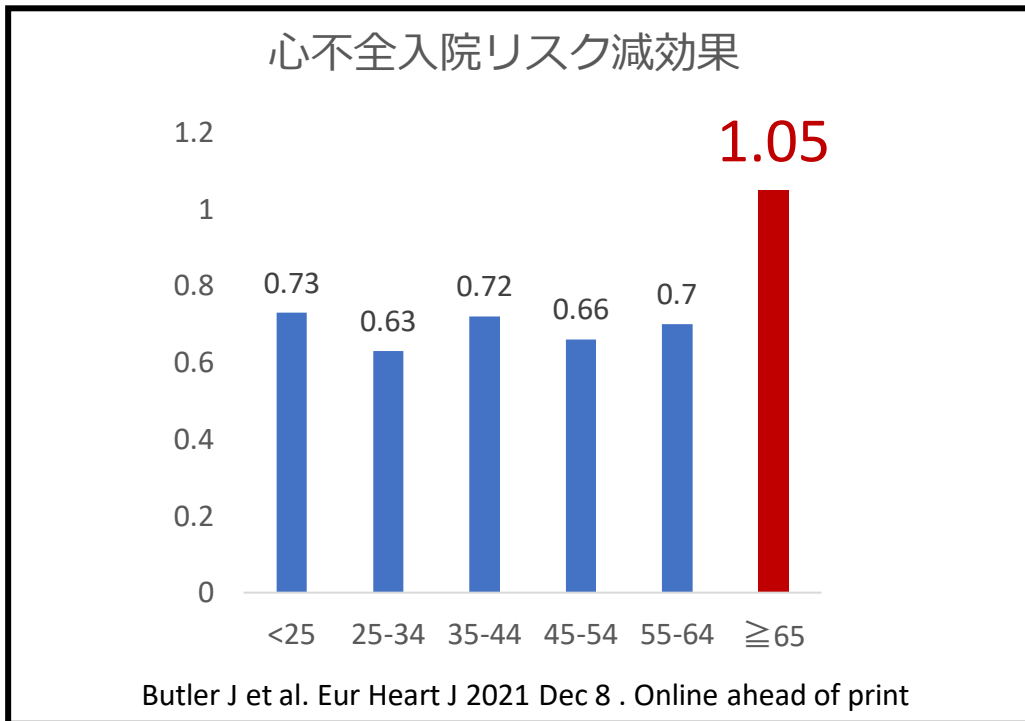


2021年 JCS/JHFS ガイドライン フォーカスアップデート版 急性・慢性心不全診療

JCS/JHFS 2021 Guideline Focused Update on Diagnosis and Treatment of Acute and Chronic Heart Failure

「急性・慢性心不全診療ガイドライン（2017年改訂版）」からあらたな知見をまとめ、フォーカスアップデートとして作成した。

HFpEFにも効果的な治療は
十分確立していない
SGLT 2 阻害薬は？
(EMPEROR-Preserved)



* 日本循環器学会, 日本心不全学会. 急性・慢性心不全診療ガイドライン (2017年改訂版)²⁾. P. 79 図11参照

*¹ ACE 阻害薬 / ARB 投与例で ARNI への切替えを考慮可

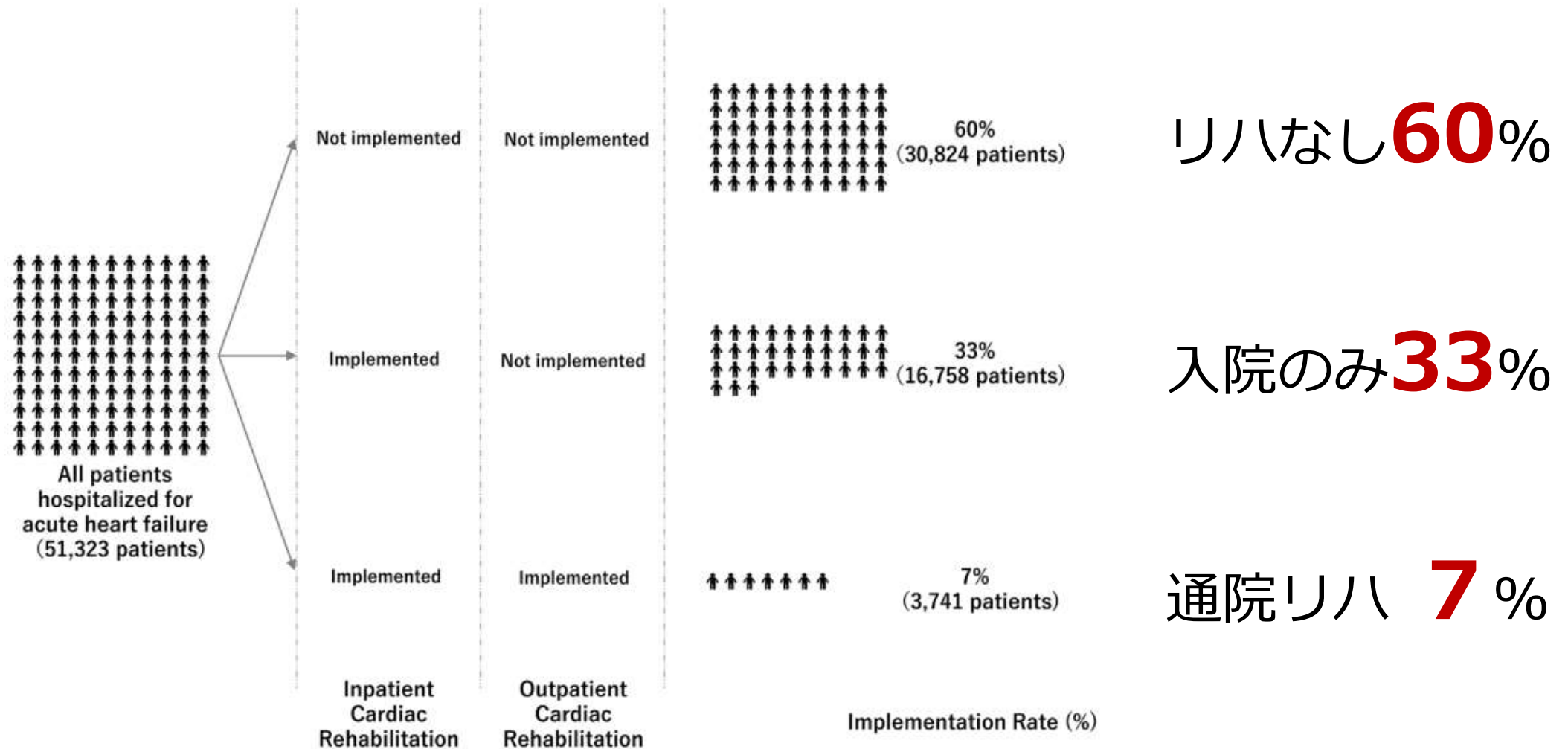
*² ACE 阻害薬 / ARB 未使用で入院例への導入も考慮 (ただし, 保険適用外)

*³ 機能性, 重症僧帽弁逆流, EF ≥ 20%



AMED-CHF

Kamiya K et al. Circ J 2019;83:1546-1552 270施設 51,323例対象



Class I Evidence level A

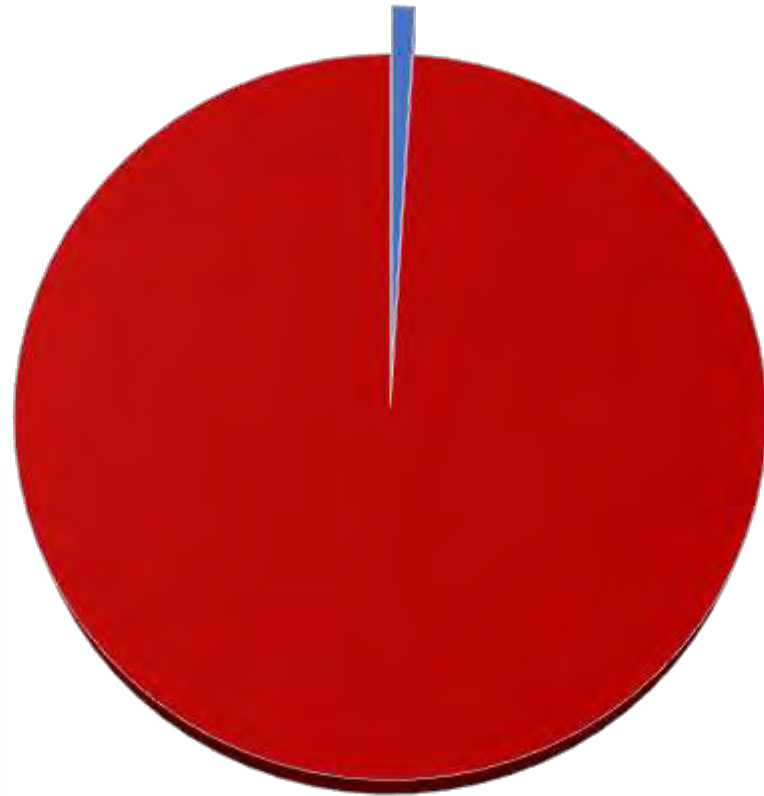
さらに**7%**のその実態は...

週3
1割

週1
9割



たった0.7%



■ 実施 ■ 未実施





Trends in the Use of Cardiac Rehabilitation in Japan Between 2010 and 2017 — An Epidemiological Survey —

Natsuko Kanazawa, PhD; Sumio Yamada, PhD; Kiyohide Fushimi, MD, PhD

高齢者 入院は増、外来は減

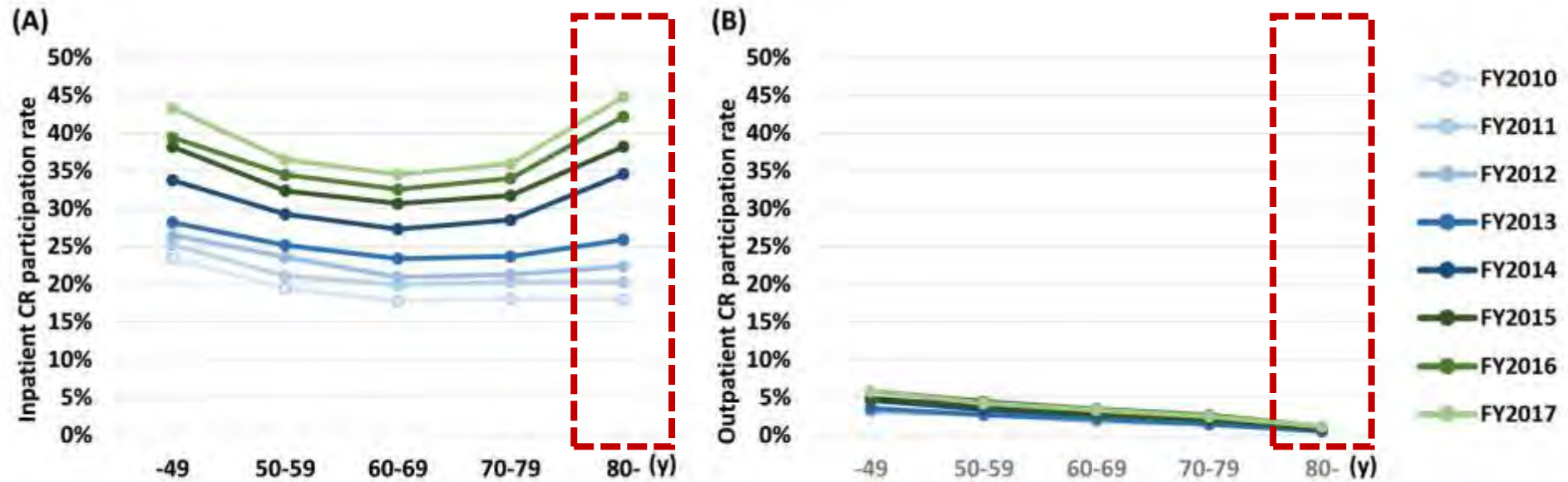


Figure 3. Changes in the relationship between (A) inpatient and (B) outpatient cardiac rehabilitation (CR) participation rates and age in each fiscal year.



心リハ障害因子

医療保険制度
心臓、患者の状態
医療者からの勧め
患者の参加意欲
プログラムの価値
時間的制約



心臓リハ 医師の役割

医師に求められるべき技能と能力

医師自ら承認する

スタッフを活かし護る

組織構築する



なぜリハが必要かを語り、
現場で参加努力を承認するのは
医師の仕事



ご興味があれば

心臓リハビリを実施する医療スタッフに求められる知識・技能・能力とは何か？

PD-4 患者とスタッフの心に灯をともす能力 ～医師こそが START WITH WHY を語れ～

Lighting Up the Hearts of Patients and Staff: Why Doctors Should "Start With Why"

勝木達夫



薬も運動も**同じ**治療です。
気が向いた時だけ薬を飲みますか？
天気が良いときだけ薬を飲みますか？



演者の個人的見解

Cardiac rehabilitation referral, attendance and mortality in women

Jillian D Colbert¹, Billie-Jean Martin^{1,2}, Mark J Haykowsky³, Trina L Hauer², Leslie D Austford⁴, Ross A Arena^{2,5}, Merril L Knudtson¹, Donald AN Meldrum^{1,2,4}, Sandeep G Aggarwal^{1,2,4} and James A Stone^{1,2,4}

HFpEFこそ効くのに
女性の心リハ参加推奨、完遂が有意に少
参加推奨 31.1% vs 42.2%
完遂 50.1% vs 60.4%

Class I Evidence Level Aの
選択肢を提示もしないのは？



やったら男性よりも女性の成績が良い
勧められなかったら男性より成績悪い

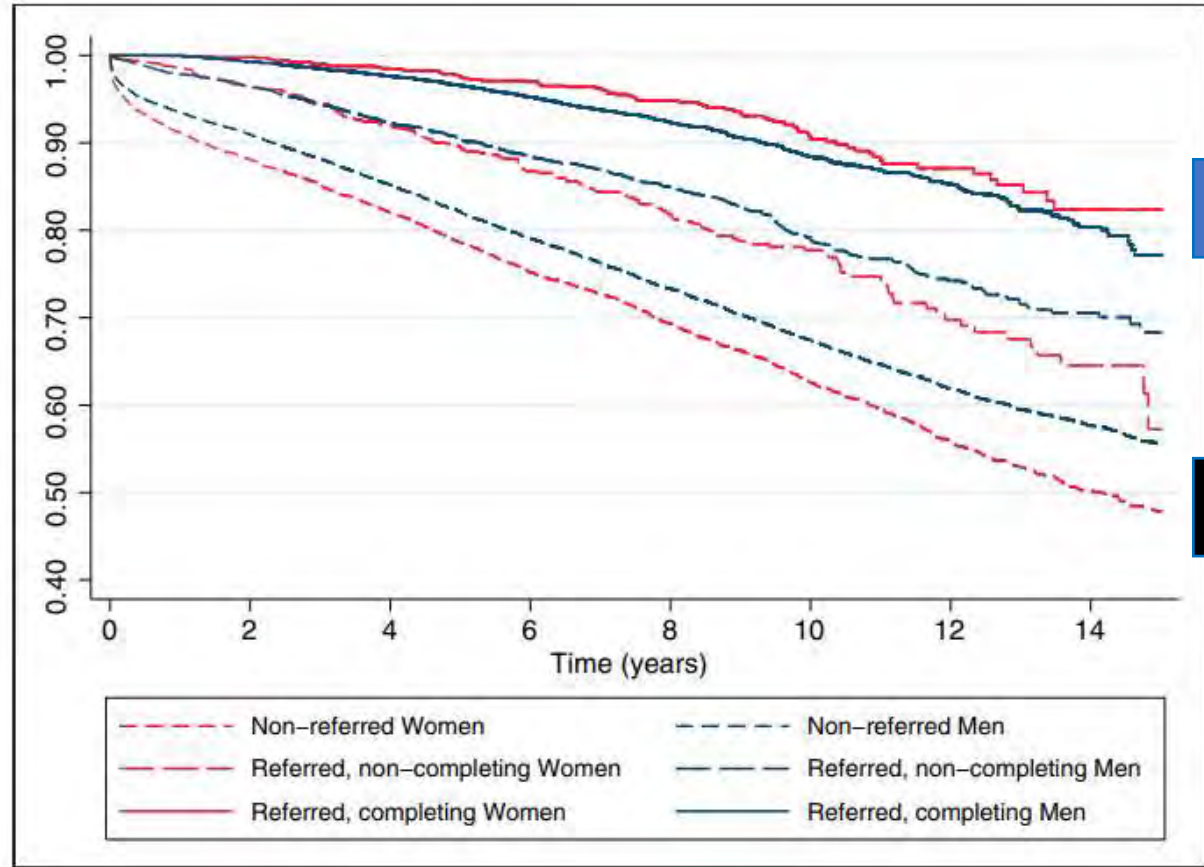


Figure 2. Survival stratified by referral, attendance and sex. Subjects classified as having never been referred, been referred but not completing CR, or having been referred and completed CR. For all survival models, subjects who were never referred to CR were the referent group.

Cardiac rehabilitation referral, attendance and mortality in women

Jillian D Colbert¹, Billie-Jean Martin^{1,2}, Mark J Haykowsky³,
Trina L Hauer², Leslie D Austford⁴, Ross A Arena^{2,5},
Merril L Knudtson¹, Donald AN Meldrum^{1,2,4},
Sandeep G Aggarwal^{1,2,4} and James A Stone^{1,2,4}



誰一人取り残すことなく

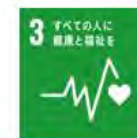


Table 3. Hazard ratios for survival associated with cardiac rehabilitation referral and completion. Non-referred subjects are the reference group.

	Women	Men
	Adjusted hazard ratio (95% CI)	Adjusted hazard ratio (95% CI)
CR status		
Referred, did not complete	0.82 (0.70, 0.97)	0.86 (0.78, 0.94)
Completed	0.36 (0.28, 0.45)	0.51 (0.46, 0.56)



Current Medical and Social Issues for Hospitalized Heart Failure Patients in Japan and Factors for Improving Their Outcomes

— Insights From the REAL-HF Registry —

Toshiro Kitagawa, MD, PhD; Takayuki Hidaka, MD, PhD; Makiko Nakai; Susumu Nakayama; Kanako Yuge; Mitsuaki Isohe, MD, PhD; Yasuki Kihara, MD, PhD for the REAL-HF Investigators

外来リハ

外来心リハを導入だけでは
予後に差がない

外来心リハを完遂できると
予後が良い

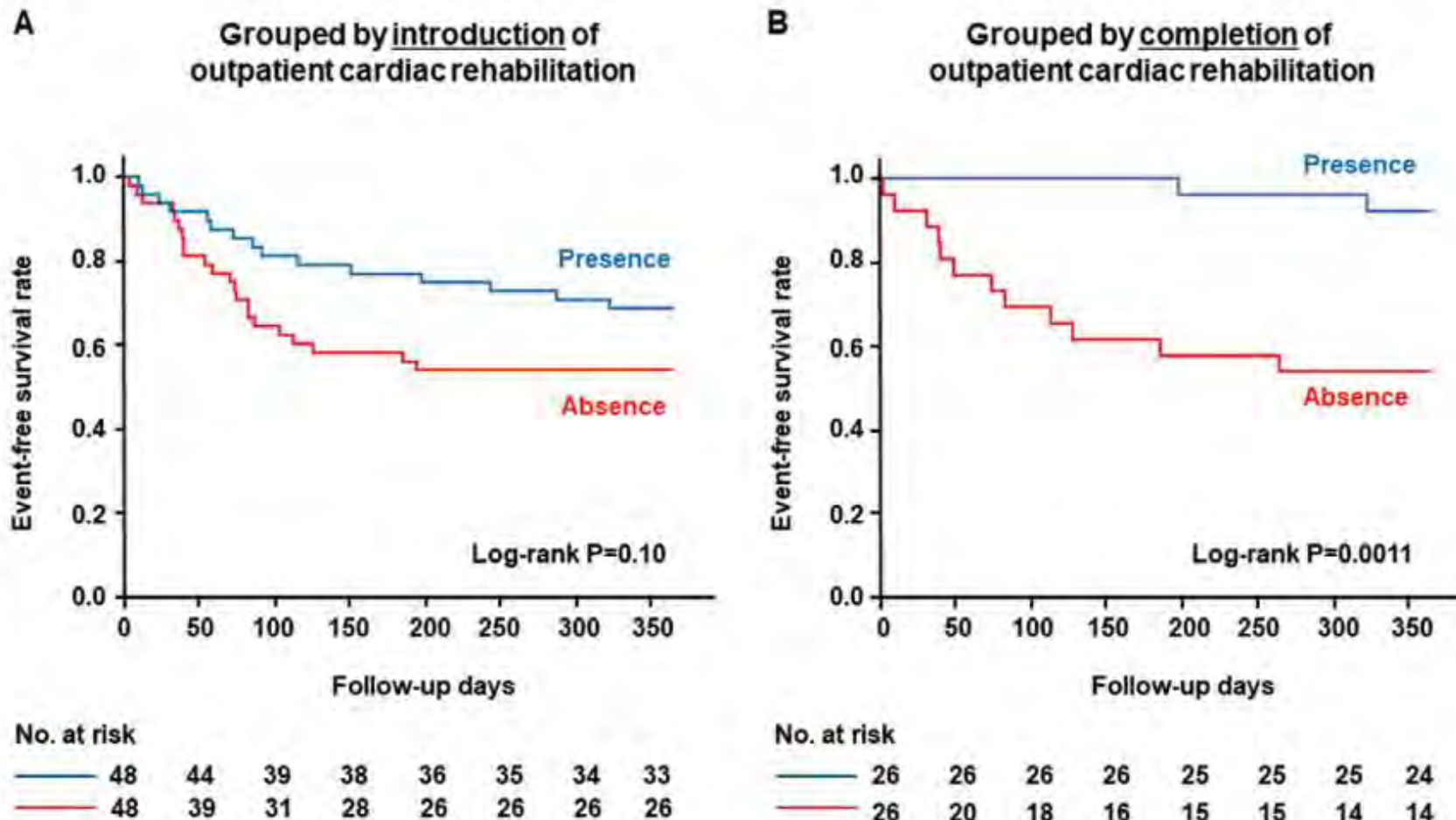


Figure 4. Kaplan-Meier curves for the primary endpoint stratified by (A) introduction or (B) completion of outpatient cardiac rehabilitation. The groups were created using propensity-matched analysis.



Current Medical and Social Issues for Hospitalized Heart Failure Patients in Japan and Factors for Improving Their Outcomes — Insights From the REAL-HF Registry —

Toshiro Kitagawa, MD, PhD; Takayuki Hidaka, MD, PhD; Makiko Naka; Susumu Nakayama; Kanako Yuge; Mitsuaki Isobe, MD, PhD; Yasuki Kitahara, MD, PhD for the REAL-HF Investigators

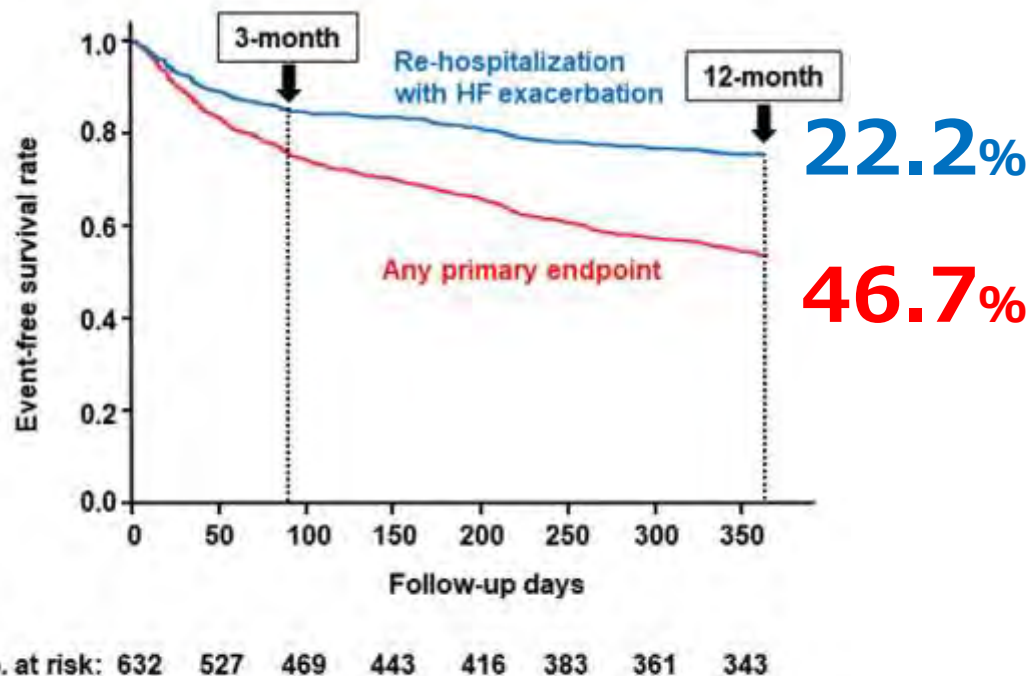


Figure 2. Kaplan-Meier curves for the primary endpoint (rehospitalization with heart failure (HF) exacerbation and any primary event) in patients discharged home.

Background: We investigated the current medical and social conditions and outcomes of heart failure (HF) patients in Hiroshima Prefecture, a local district in Japan.

Methods and Results: From March 2017 to February 2018 we enrolled all adult patients with hospitalized HF in 8 regional core hospitals that provided an interprofessional team approach for HF patients. We collected patients' clinical characteristics and information regarding living circumstances, cognitive function, quality of life, and interprofessional team approach. For patients discharged home, we followed up the primary endpoint (all-cause death and all-cause unscheduled readmission), conditions of outpatient cardiac rehabilitation, and home nursing-care services over a 1-year period after discharge. Of the registered patients (n=1,218), 39.2% were super-elderly (≥ 85 years old); more than half of these patients had preserved ejection fraction ($\geq 50\%$). In the follow-up cohort (n=632), 140 patients (22.2%) were readmitted with HF exacerbation as the primary endpoint, and almost half (n=295, 46.7%) experienced any primary endpoint. The multivariate analysis adjusted for medical and social factors showed that completion of outpatient cardiac rehabilitation (5-month program) remained a strong negative predictor of the primary endpoint (hazard ratio: 0.15; 95% confidence interval: 0.05–0.48; $P=0.0013$).

Conclusions: Our cohort study highlighted the super-aging of current HF patients in Japan. Cardiac rehabilitation through continuous team approach appears to be associated with favorable overall outcomes in this population.

Primary endpoint 全死亡、全予定外入院

39.2% 85歳以上
半数以上はEF $\geq 50\%$

5か月の心リハ **完遂** でリスク低下 **85%**



心リハ障害因子

医療保険制度
心臓、患者の状態
医療者からの勧め
患者の参加意欲
プログラムの価値
時間的制約



KEEP OUT KEEP OUT KEEP OUT
KEEP OUT KEEP OUT KEEP OUT



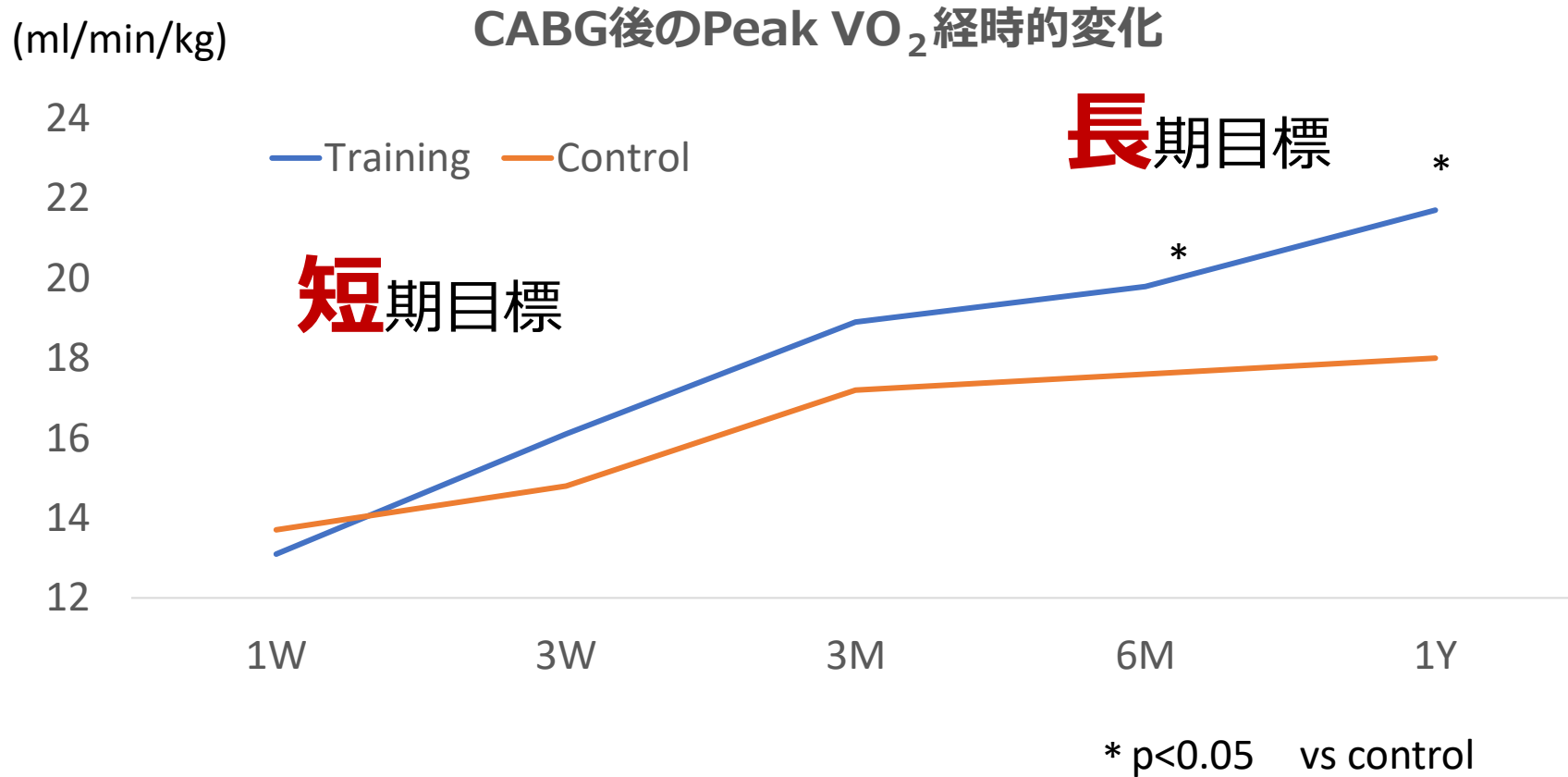
Effects of Physical Training on the Recovery of the Autonomic Nervous Activity During Exercise After Coronary Artery Bypass Grafting
 — Effects of Physical Training After CABG —

Junichiro Takeyama, MD*; Haruki Itoh, MD; Makoto Kato, MD;
 Akira Koike, MD; Keiichi Aoki, MD; Long Tai Fu, MD;
 Hiroshi Watanabe, MD; Masatoshi Nagayama, MD*; Takashi Katagiri, MD*

Table 2 Changes in the Anaerobic Threshold, Peak $\dot{V}O_2$ and Body Weight

	1 week	3 weeks	3 months	6 months	1 year
<i>Anaerobic threshold (ml·min⁻¹·kg⁻¹)</i>					
Training group	10.6±1.6	11.9±1.6*	13.2±1.6*	13.6±1.0*	14.4±2.1*
Control group	11.6±1.3	11.4±1.5	12.5±1.9	13.1±1.3*	13.2±0.9*
<i>Peak $\dot{V}O_2$ (ml·min⁻¹·kg⁻¹)</i>					
Training group	13.1±1.7	16.1±2.0*	18.9±2.5*	19.8±2.8*†	21.7±2.6*†
Control group	13.7±2.5	14.8±2.3	17.2±2.8*	17.6±2.4*	18.0±2.0*
<i>Body weight (kg)</i>					
Training group	64.3±6.3	62.3±6.8	64.0±6.4	64.9±6.4	64.2±7.0
Control group	63.2±10.7	59.8±8.6	66.7±10.2	64.5±10.9	65.3±12.1

Values are expressed as the mean±SD. *p<0.05 vs 1 week, †p<0.05 vs Control group.



術直後の体力低下は皆起きることを術前から繰り返し説明
 長期の見通しを示す



ORIGINAL RESEARCH

Dose of Cardiac Rehabilitation to Reduce Mortality and Morbidity: A Population-Based Study

José R. Medina-Inojosa, MD, MSc; Sherry L. Grace, PhD; Marta Supervia, MD, MSc; Gorazd Stokin, MD, PhD; Amanda R. Bonikowski, PhD; Randal Thomas, MD, MSc; Francisco Lopez-Jimenez, MD, MSc

BACKGROUND: There is wide variability in cardiac rehabilitation (CR) dose (ie, number of sessions) delivered, and no evidence-based recommendations regarding what dose to prescribe. We aimed to test what CR dose impacts major adverse cardiovascular events (MACEs).

METHODS AND RESULTS: This is an historical cohort study of all patients who had coronary artery disease and who initiated supervised CR between 2002 and 2012 from a single major CR center. CR dose was defined as number of visits including exercise and patient education. Follow-up was performed using record linkage from the Rochester Epidemiology Project. MACEs included acute myocardial infarction, unstable angina, ventricular arrhythmias, stroke, revascularization, or all-cause mortality. Dose was analyzed in several ways, including tertiles, categories, and as a continuous variable. Cox models were adjusted for factors associated with dose and MACE. The cohort consisted of 2345 patients, who attended a mean of 12.5±11.1 of 36 prescribed sessions. After a mean follow-up of 6 years, 695 (29.65%) patients had a MACE, including 231 who died. CR dose was inversely associated with MACE (hazard ratio, 0.66 [95% CI, 0.55–0.91] in those completing ≥20 sessions, when compared with those not exposed to formal exercise sessions (≤1 session; log-rank $P=0.007$). We did not find evidence of nonlinearity ($P>0.050$), suggesting no minimal threshold nor ceiling. Each additional session was associated with a lower rate of MACE (fully adjusted hazard ratio, 0.98 [95% CI, 0.97–0.99]). Greater session frequency was also associated with lower MACE risk (fully adjusted hazard ratio, 0.74 [95% CI, 0.58–0.94]).

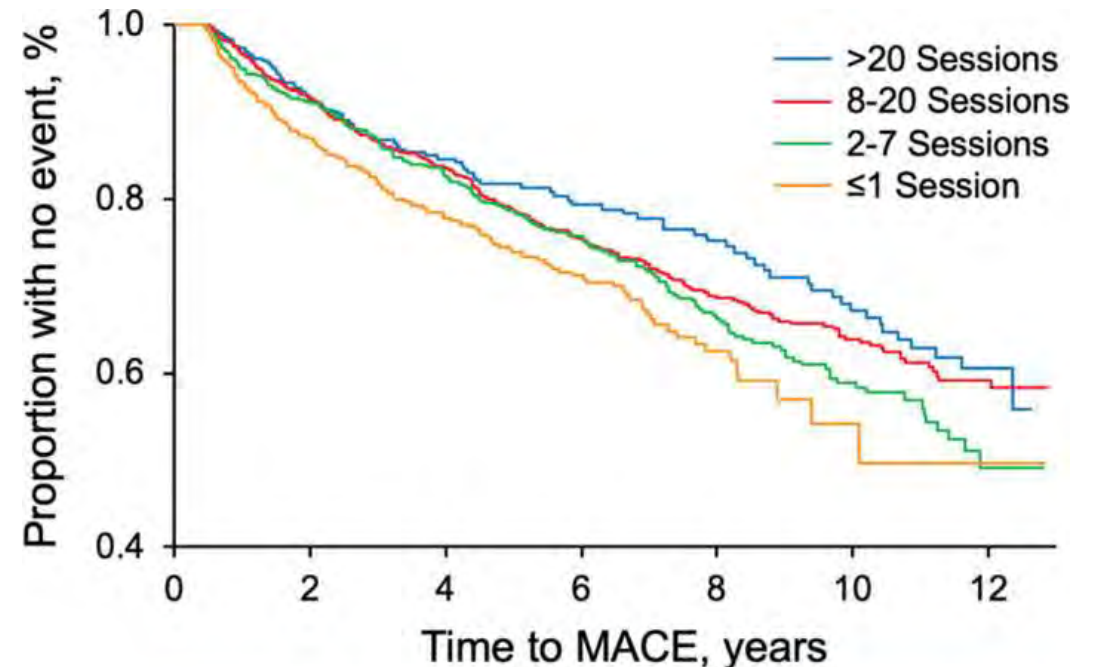
J Am Heart Assoc. 2021;10:e021356. DOI: 10.1161/JAHA.120.021356

予定36セッションへの平均参加12.5回
45分運動 + 15分教育カウンセリング
12週間

平均 6 年フォロー、MACE30%発生

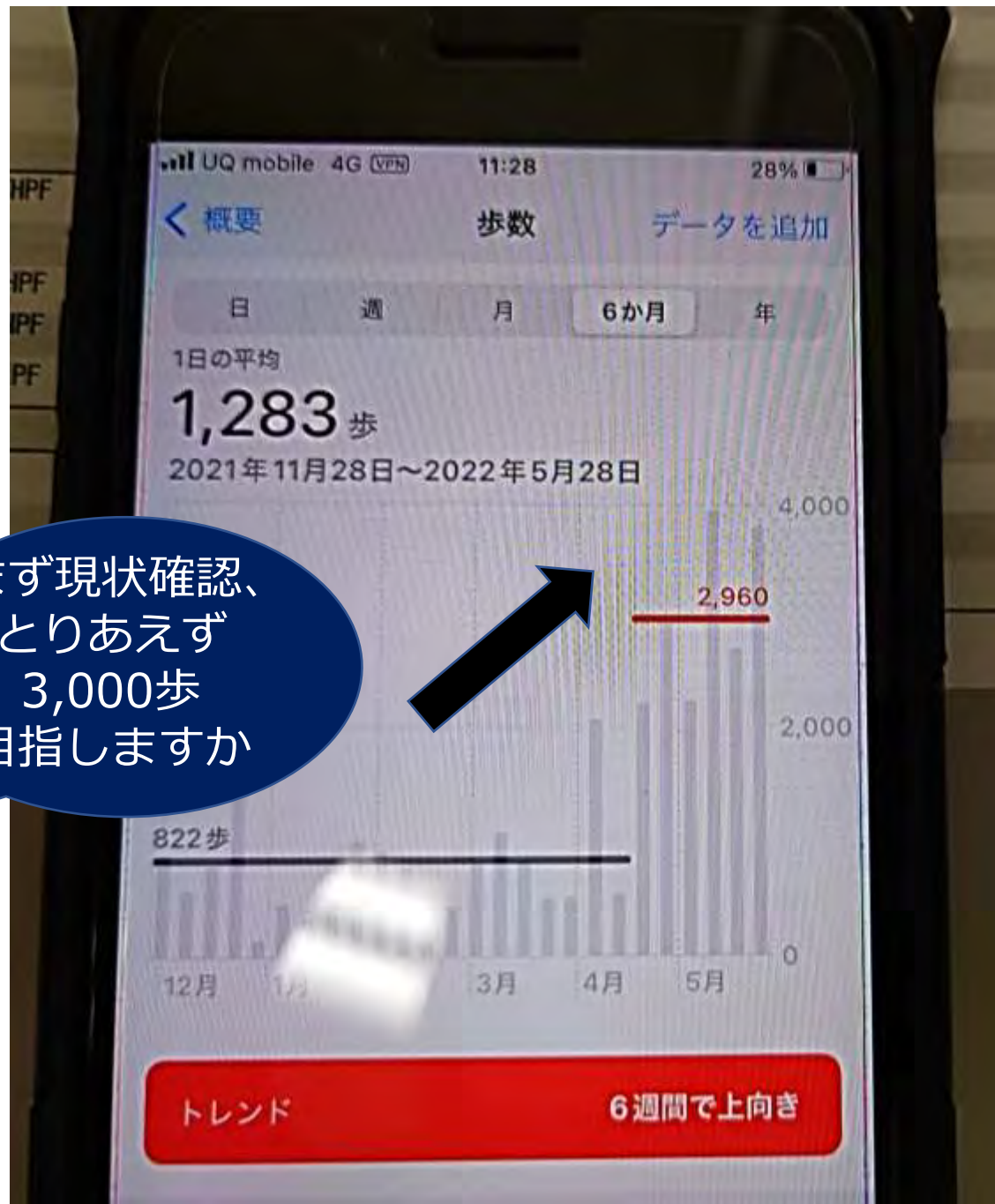
20回以上の参加は1回以下に比し34%減
($p=0.007$)

参加回数の効果上限はなし



Log-Rank p-value 0.007





12月-3月 822歩



4月に入ってから徐々に
非監視型運動量が増加
4月後半から 2,960歩



毎日の記録 CPX

年		日	月	火	水	木	金	土
月/日		7/31	8/1	2	3	4	5	6
体重(kg)		72.8	72.6	73.0	73.6	74.0	74.4	74.6
血圧 (mmHg)	朝 (脈拍回/分)	128/54 (59)	133/64 (59)	129/67 (60)	130/59 (60)	133/58 (60)	139/57 (58)	129/64 (60)
	寝る前 (脈拍回/分)	110/52 (62)	103/48 (58)	127/55 (69)	113/57 (60)	130/55 (59)	122/50 (62)	115/50 (58)
自覚症状	息切れ	有・無	有・無	有・無	有・無	有・無	有・無	有・無
	むくみ	有・無	有・無	有・無	有・無	有・無	有・無	有・無
	疲れやすさ	有・無	有・無	有・無	有・無	有・無	有・無	有・無
	食欲低下	有・無	有・無	有・無	有・無	有・無	有・無	有・無
	不眠	有・無	有・無	有・無	有・無	有・無	有・無	有・無
運動(回かXで記入)		6824	6896	3847	8070	868	2264	6854
服薬 チェック	朝	✓	✓	✓	✓	✓	✓	✓
	昼	✓	✓	✓	✓	✓	✓	✓
	夕	✓	✓	✓	✓	✓	✓	✓

毎日の記録

年		日	月	火	水	木	金
月/日		8/7	8	/	/	/	/
体重(kg)		74.6	74.4				
血圧 (mmHg)	朝 (脈拍回/分)	131/63 (60)	138/64 (60)	/	/	/	/
	寝る前 (脈拍回/分)	118/59 (59)	/	/	/	/	/
自覚症状	息切れ	有・無	有・無	有・無			
	むくみ	有・無	有・無	有・無			
	疲れやすさ	有・無	有・無	有・無			
	食欲低下	有・無	有・無	有・無			
	不眠	有・無	有・無	有・無			
運動(回かXで記入)		7539					
服薬 チェック	朝	✓	✓	□	□	□	□
	昼	✓	✓	□	□	□	□
	夕	✓	✓	□	□	□	□

8月には、
6,000-8,000歩

「変わる」に
気づく、讚える、
支援する

記録の確認は
努力の承認



心リハ障害因子

医療保険制度
心臓、患者の状態
医療者からの勧め
患者の参加意欲
プログラムの価値
時間的制約



KEEP OUT KEEP OUT KEEP OUT
KEEP OUT KEEP OUT KEEP OUT



RESEARCH ARTICLE

Open Access



The use of geographical analysis in assessing the impact of patients' home addresses on their participation in outpatient cardiac rehabilitation: a prospective cohort study

Atsuko Nakayama^{1,2*}, Masatoshi Nagayama², Hiroyuki Morita^{1*}, Takuya Kawahara², Issei Komuro¹ and Mitsuaki Isobe²

距離が遠いと
始まらない
続かない

CABG例
<10kmと ≥ 30 kmで
開始半減、脱落4倍

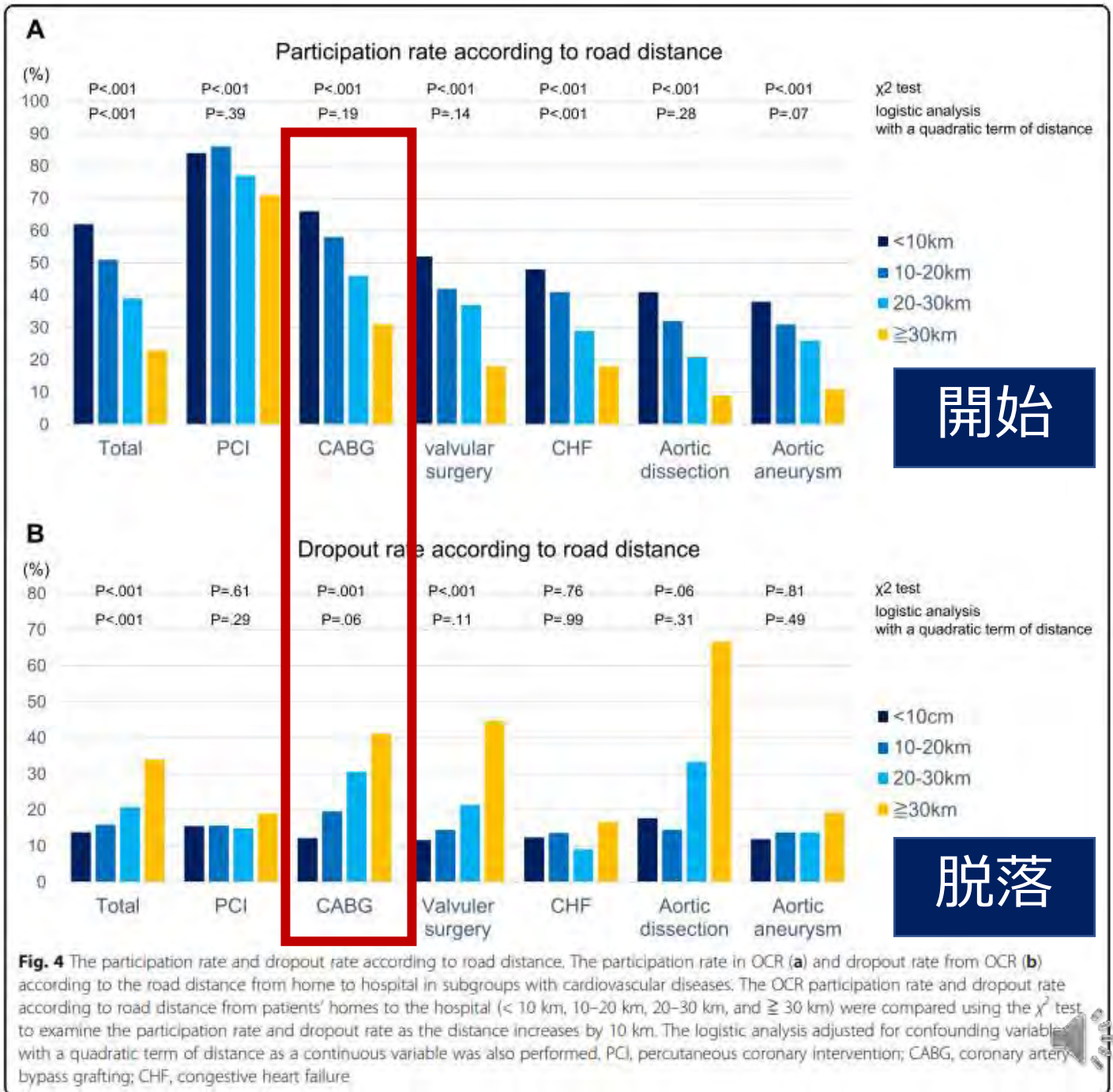


Fig. 4 The participation rate and dropout rate according to road distance. The participation rate in OCR (a) and dropout rate from OCR (b) according to the road distance from home to hospital in subgroups with cardiovascular diseases. The OCR participation rate and dropout rate according to road distance from patients' homes to the hospital (< 10 km, 10–20 km, 20–30 km, and ≥ 30 km) were compared using the χ^2 test to examine the participation rate and dropout rate as the distance increases by 10 km. The logistic analysis adjusted for confounding variables with a quadratic term of distance as a continuous variable was also performed. PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CHF, congestive heart failure



高齢者の免許返納
通院困難事例

外来リハ障害因子

↓

送迎可能な

通所リハビリテーション

Worcester MUC, et al. Cardiac rehabilitation programmes:
predictors of non-attendance and drop-out.
Eur J Cardiovasc prev rehabil. 2004;11:328-335.

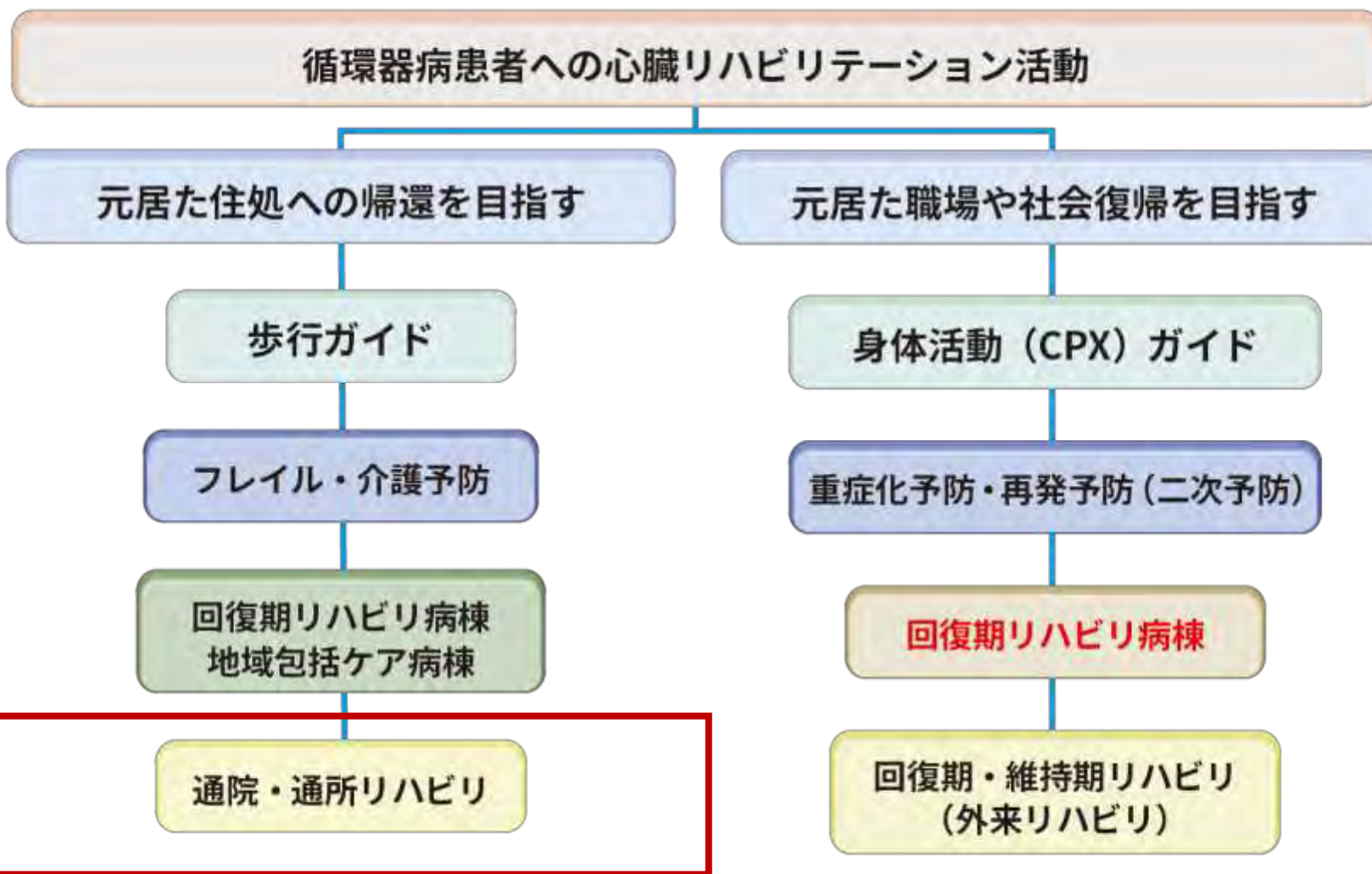


循環器病患者への心臓リハビリテーション活動

対象は
わけて
考える

急性期で
完結せず

介護保険
活用



社会資源を活用する。	I	A	A	I
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介護保険サービスと開始時期 2週以内が成績良いが、半数のみ

退院後の通所リハビリテーション利用開始までの期間と開始後のADL向上

退院後から通所リハビリテーションを利用開始するまでの期間が短いほど、機能回復が大きい傾向が見られた。

退院から通所リハビリテーション開始までの日数



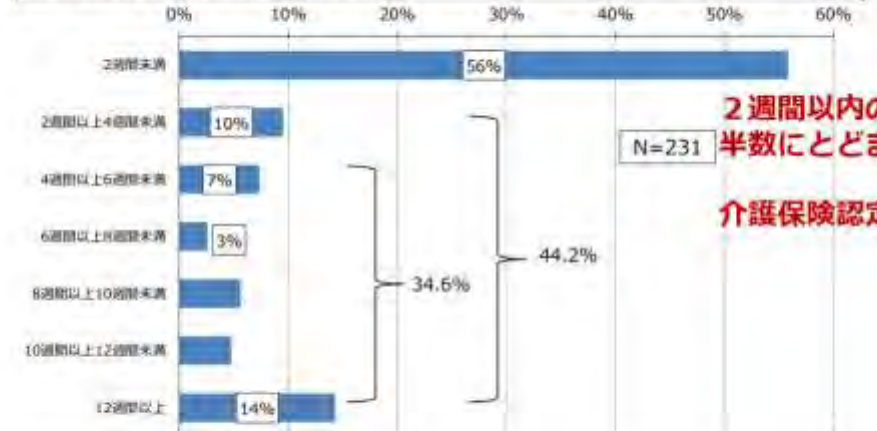
※平成27年10月以降に退院した者231名について集計

(出典) 平成27年度介護報酬改定検証調査(平成28年度調査)の結果を事務局で集計 43

https://www.mhlw.go.jp/file/05-Shingikai-12601000-Seisakutoukatsukan-Sanjikanshitsu_Shakaihoshoutantou/0000168706.pdf

退院後の通所リハビリテーション利用開始までの期間

退院後に通所リハビリテーションの利用を開始した者の44.2%は、退院から通所リハビリテーションの利用開始まで2週間以上かかっており、34.6%は4週間以上かかっていた。



※平成27年10月以降に退院した者231名について集計

(出典) 平成27年度介護報酬改定検証調査(平成28年度調査)の結果を事務局で集計 42

https://www.mhlw.go.jp/file/05-Shingikai-12601000-Seisakutoukatsukan-Sanjikanshitsu_Shakaihoshoutantou/0000168706.pdf



介護予防・日常生活支援総合事業 ガイドライン(概要)

厚生労働省老健局振興課

迅速に介入 基本チェックリストで判定

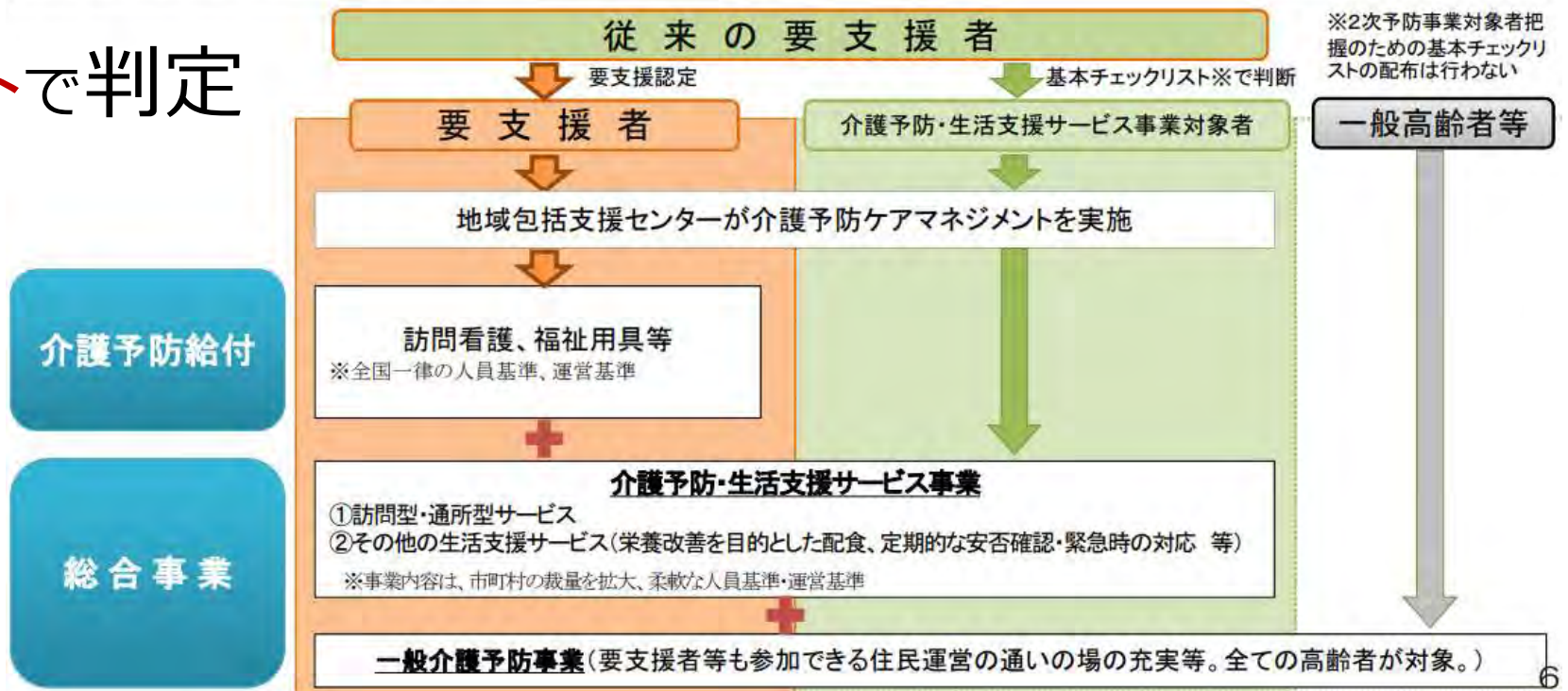
介護申請
総合事業



第1 総合事業に関する総則的な事項

【参考】総合事業の概要

- 訪問介護・通所介護以外のサービス(訪問看護、福祉用具等)は、引き続き介護予防給付によるサービス提供を継続。
 - 地域包括支援センターによる介護予防ケアマネジメントに基づき、総合事業(介護予防・生活支援サービス事業及び一般介護予防事業)のサービスと介護予防給付のサービス(要支援者のみ)を組み合わせる。
 - 介護予防・生活支援サービス事業によるサービスのみ利用する場合は、要介護認定等を省略して「介護予防・生活支援サービス事業対象者」とし、迅速なサービス利用を可能に(基本チェックリストで判断)。
- ※ 第2号被保険者は、基本チェックリストではなく、要介護認定等申請を行う。



総合事業（短期集中予防サービス） 介護保険を用いない

お住いの自治体（市町村）に 対象疾患や、価格等の確認を

通所介護C（短期集中予防サービス）市町村総合事業

通所系サービスとして現行の通所介護のほか、
通所介護A（基準緩和型サービス）、通所介護B（住民主体による支援）、通所介護C（短期集中予防サービス）

通所介護C（短期集中予防サービス）

①対象者
ADLやIADLの改善に向けた支援が必要なケース

②サービス内容
生活機能を改善するための運動器の機能向上や栄養改善等のプログラムを提供、
送迎あり、入浴無し、交流より機能訓練を目的

③開始判断
基本チェックリストで判断し、**介護保険を用いずに迅速導入**
実施方法は市町村の直接事業の場合と委託の場合あり

④提供者
保健・医療の専門職

⑤期間
3～6ヶ月の短期間で実施

小松市の特徴

①入退院者を対象とした入院後の機能低下改善
（生活行為の再自立）として実施

②訪問支援は利用者負担なし

③サービス利用回数は介護度等による固定ではなく、
多職種で必要量を相談して柔軟に決定

④多職種でのチーム会議を毎月実施

⑤1回利用料が500円と安価、の5点



第28回日本心臓リハビリテーション学会学術集会 P-193

短期集中予防サービスを活用する 退院後の心臓リハビリテーションアプローチ

特定医療法人社団勝木会やわたメディカルセンター
勝木達夫 循環器内科

岩佐和明 リハビリテーション技師部理学療法課
今井美里 リハビリテーション技師部理学療法課
山口宏美 事務部診療情報管理課

公立小松大学保健医療学部
山崎松美



日本心臓リハビリテーション学会誌 under review

身体機能・組成項目	転入院時	退院/短集S開始時	終了時
歩行速度(m/s)	1.0	1.3	2.0
握力(kg)	20	20	23
膝伸筋筋力体重比(%)	50	51	57
SPPB	7	11	-
6分間歩行距離(m)	335	425	465
体重(kg)	55.3	54.7	58.0
筋肉量(kg)	-	38.1	40.1
		PeakVO ₂ /weight 12.3ml/kg/min	
KCL項目			
社会参加	2	5*	2
運動器	3*	3*	0
栄養	1	0	0
口腔	0	0	0
閉じこもり	2*	2*	1*
物忘れ	0	0	0
うつ	5*	3*	3*
計	13	13	6

SPPB: Short Physical Performance Battery 短集S: 短期集中予防サービス
KCL: 基本チェックリスト *KCLによる短期集中予防サービス利用対象に該当する項目

心リハ障害因子

医療保険制度
心臓、患者の状態
医療者からの勧め
患者の参加意欲
プログラムの価値
時間的制約

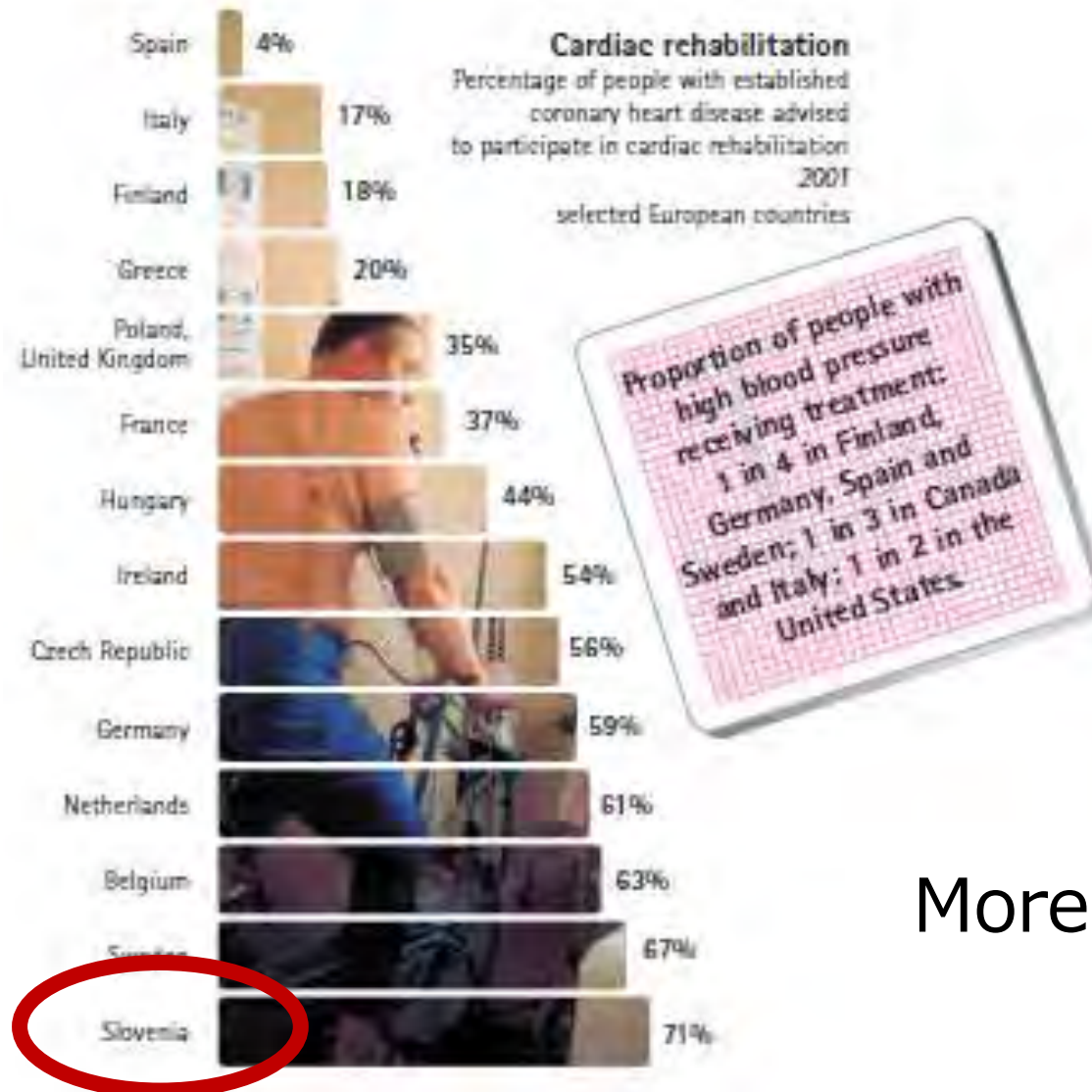


KEEP OUT KEEP OUT KEEP OUT
KEEP OUT KEEP OUT KEEP OUT



Slovenia

One of the **highest** participation rates in Europe



More than **40** years



家族を巻き込み、体感を共有する In Slovenia



To **share** the same diet and exercise experience, **30%** of the patients bring their **spouses** with them in **Slovenia**.



Hotel Stay

Not hospitalized to receive rehabilitation

Nestled in a natural setting

State-managed special clinic attached to the hotel



Daily activities

7:30AM **Aquatic** exercise(30min)

-Breakfast-

10:30AM **Nordic** Walking(45min)

11:00AM Walking mini-**excursion**(15minx2)

-Lunch-

Ergometer

Chair exercise

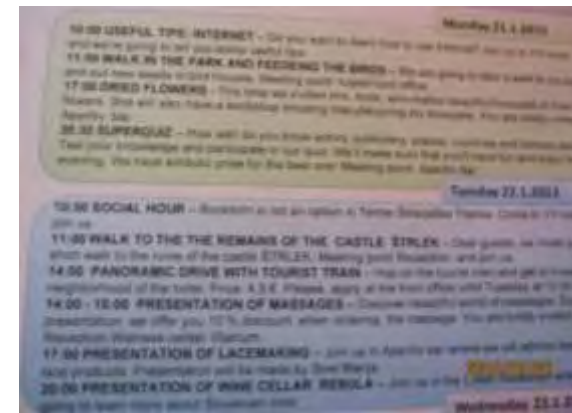
Culture Class

(Dried flower, Lacemaking, Massage etc)

-Dinner-

Entertainment Event

(Yoga class, Cellar wine tasting, **Dance** class etc)





Healthcare for all

Governmental Healthcare

Provide assistance in going back to work

Pay **80%** of the income lost during the time out of work





Postoperative CR Commonsense Culture

2012
Open heart surgery 919 cases
Device 854 cases
Ave.hospital stay 7.92d





Thermal Resort Therapy

Onsen

演者の個人的見解



心臓リハ 医師の役割

医師に求められるべき技能と能力

医師自ら承認する

スタッフを活かし護る

組織構築する



チームの活躍する舞台づくり



ご興味があれば

ハウツーセッション 1：心臓リハビリの立ち上げと運営

心臓リハビリの立ち上げと運営（まとめ）

Setup and administration of the cardiac rehabilitation

やわたメディカルセンター 循環器内科 勝木達夫
岡山大学大学院医歯薬学総合研究科 機能制御学講座循環器内科 伊藤 浩

【心臓リハビリテーション (JJCR) 17 (1) : 64-67, 2012】



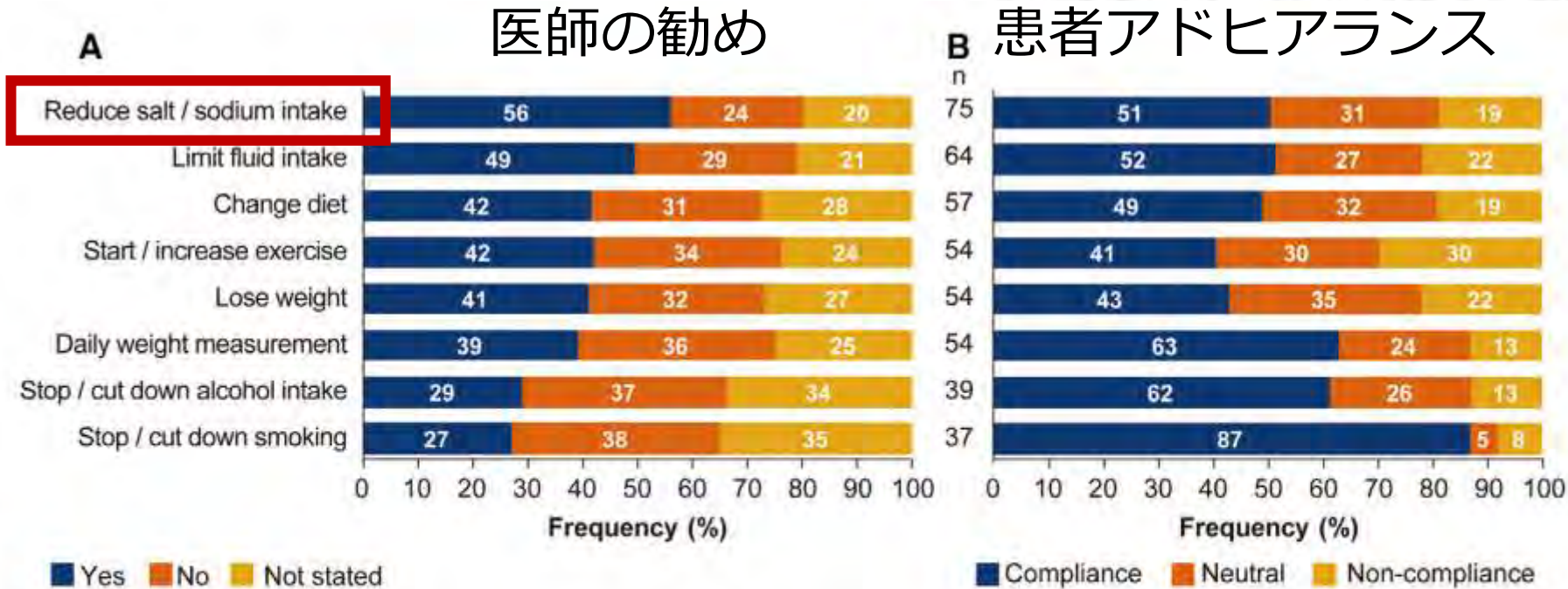
Burden of Heart Failure on Patient Daily Life and Patient–Physician Discordance in Disease Management — Results From a Cross-Sectional Survey in Japan —

Tomoko Hayashi, PhD; Yohei Morita, MD; Hironobu Mitani, PhD; Hiroki Murayama, PhD; Toshinori Anzai, MD, PhD; Rachel Studer, PhD; Sarah Cotton; James Jackson; Hollie Bailey, BSc; Hiroshi Kitagawa, MD, PhD; Naotatsu Oyama, MD, PhD

Background: We investigated the impact of heart failure (HF) on daily life and satisfaction with current HF medication from the patient perspective in a real-world study in Japan.

Methods and Results: A cross-sectional survey of 154 HF patients treated by 58 cardiologists was conducted in Japan using patient self-completed questionnaires about their daily life and satisfaction with HF medication, as well as patient record forms completed by their physicians capturing corresponding data. The mean age of patients was 72.7 years. The proportion of patients within New York Heart Association Class I, II, III, and IV was 39%, 44%, 16%, and 1%, respectively. Symptoms reported by patients included dyspnea when active (46%), nocturia (43%), anxiety (18%), and depression (6%). There was a discordance between physician- and patient-reported symptoms, especially for nocturia and inability to sleep. The most frequent lifestyle recommendation from physicians was 'reduce salt/sodium intake', but only 51% of patients receiving this recommendation followed the advice. In all, 44% of patients reported dissatisfaction with their current medication; according to the patients, 27% reported no discussion with their physicians about their prescribed medication, while physicians reported the opposite.

Conclusions: HF negatively impacts patient daily life. There is discordance between patients and physicians in symptom reporting, lifestyle modification advice and adherence, and reported medication decision making. Gaps in patient–physician communication exist.



本気？



医師が求める減塩は
半数にしか響かず

Figure 2. (A) Lifestyle modifications recommended by physicians to their heart failure patients and (B) patient adherence to the lifestyle change among patients who received the corresponding recommendation (n=154, matched analysis of 154 physician–patient pairs; totals may not equal 100% due to rounding). Patient adherence was evaluated using a 5-point scale, where 1=no change in lifestyle at all and 5=changed lifestyle completely. Scores of 4 and 5 were pooled as 'compliance', a score of 3 represents 'neutral', and scores of 1 and 2 were pooled as 'non-compliance'.

投薬に44%が不満



Cardiac rehabilitation is a team effort 多職種協働の舞台づくり

多職種協働での 行動変容支援



ANSWERS
by heart

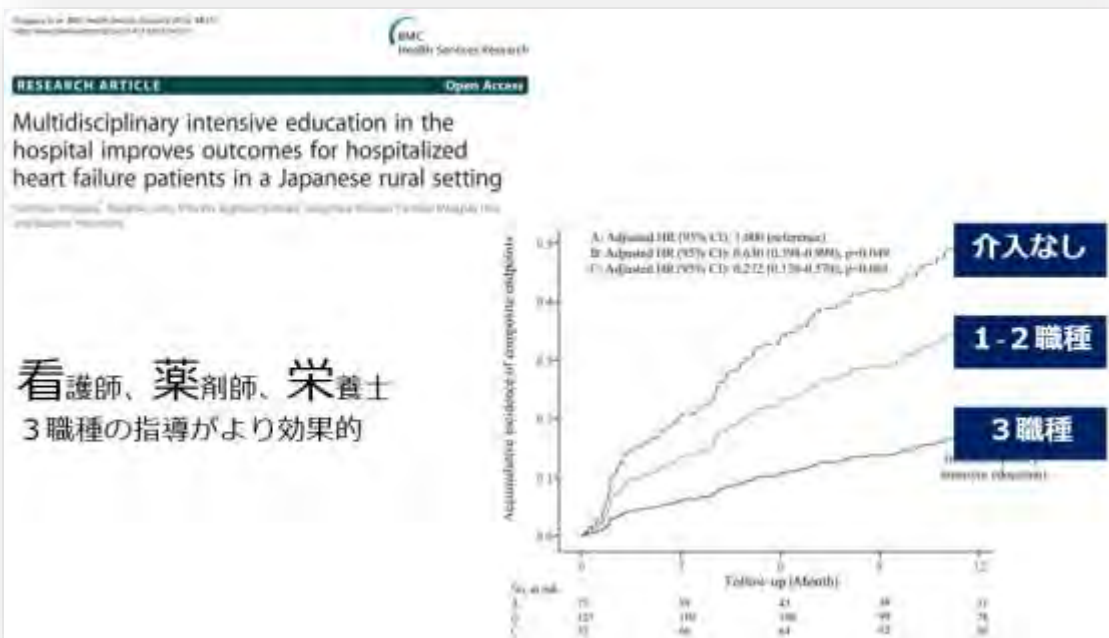


What Is Cardiac Rehabilitation?

Cardiac rehabilitation is a medically supervised program designed to improve your heart health after heart problems or surgery. It can take place at an outpatient clinic or in a hospital rehab center.

You don't have to face heart disease alone. **Cardiac rehab is a team effort** that may include doctors, nurses, exercise specialists, dietitians, nutritionists and others. Their goal is to help you make lifestyle choices to improve your heart health.

Ask your doctor if you're eligible for a cardiac rehab program. If you are, ask for a referral in your area.



[What Is Cardiac Rehabilitation? \(heart.org\)](https://www.heart.org)



塩分制限が 達成できる支援

指導ではなく支援

急性期の指導は受け入れられているか？の
再度のアセスメント



△eGFRの改善には減塩がキモ

JMAPメソッド活用



そのひと振り習慣で寿命短縮

Adding salt to foods and hazard of premature mortality

2022 Jul 10;ehac208.doi: 10.1093/eurheartj/ehac208. Online ahead of print



50歳の平均余命

塩をほぼかけない人に対して
習慣的にかける人は

女性 1.5年

男性 2.28年 寿命短縮



醤油スプレーで1/3に

とにかくダメ、ではなく、**これならよい**

紹介だけでなく、入手可能に

醤油スプレー



演者の個人的見解



調理指導ではなく入手可能 調剤薬局限定 1食で3g減

より健康を気づかう方へ

マイサイズ
いいね！プラス



おいしくて
塩分 1g

塩分が気になる方の
欧風カレー
1食100kcal、塩分1g

より塩分コントロールが
必要な方へ。
カラダを気遣う
おいしいカレーができました。

マイサイズいいね！プラスに
1食置き換えて**2~3g減**
おいしく塩分コントロール

大塚食品



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

SEPTEMBER 16, 2021

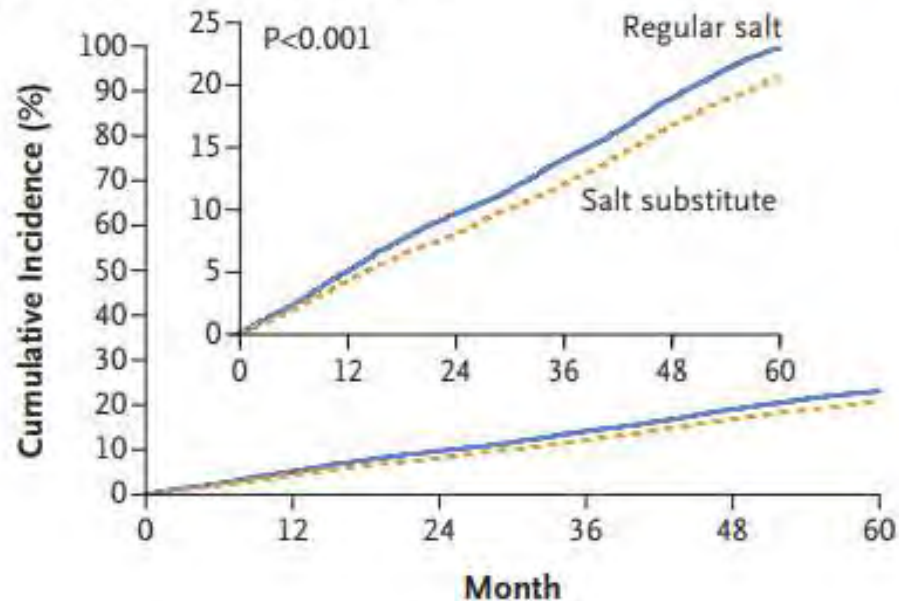
VOL. 385 NO. 12

Effect of Salt Substitution on Cardiovascular Events and Death

B. Neal, Y. Wu, X. Feng, R. Zhang, Y. Zhang, J. Shi,* J. Zhang, M. Tian, L. Huang, Z. Li, Y. Yu, Y. Zhao, B. Zhou, J. Sun, Y. Liu, X. Yin, Z. Hao, J. Yu, K.-C. Li, X. Zhang, P. Duan, F. Wang, B. Ma, W. Shi, G.L. Di Tanna, S. Stepien, S. Shan, S.-A. Pearson, N. Li, L.L. Yan, D. Labarthe, and P. Elliott

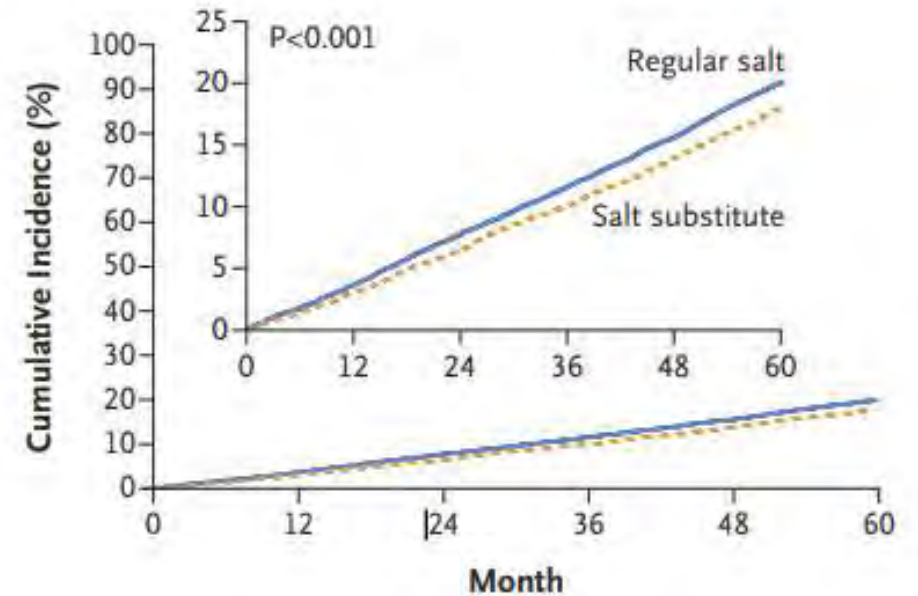
13%減($p < 0.001$)

B Major Adverse Cardiovascular Events



12%減($p < 0.001$)

C Death from Any Cause



代替塩という選択肢

塩化カリウム入り、という選択
腎機能に応じて



EDITORIAL COMMENT

Listening to Patients*

Edward P. Havranek, MD, FACC,†‡

Larry A. Allen, MD, MHS‡

Denver, Colorado

JACC2008;52:1709-1710

患者の声を聴く

LIFE : 生命のみならず生活、人生への思い
急性期を脱したら…



To elicit preferences, physicians must first have accurate knowledge not only of **expected survival** associated with therapy, but also of effects of therapy on **quality of life**.

it is important that discussions with patients about their preferences take place when they are **in a stable condition after acute exacerbations**, as outlook seems to change importantly after hospitalization.





Burden of Heart Failure on Patient Daily Life and Patient–Physician Discordance in Disease Management — Results From a Cross-Sectional Survey in Japan —

Tomoko Hayashi, PhD; Yohei Morita, MD; Hironobu Mitani, PhD; Hiroki Murayama, PhD; Toshinori Anzai, MD, PhD; Rachel Studer, PhD; Sarah Cotton; James Jackson; Hollie Bailey, BSc; Hiroshi Kitagawa, MD, PhD; Naotsugu Oyama, MD, PhD

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Conclusions: HF negatively impacts patient daily life. There is discordance between patients and physicians in symptom reporting, lifestyle modification advice and adherence, and reported medication decision making. Gaps in patient–physician communication exist.

困っていることを
医療者が把握していない

夜間頻尿 睡眠障害

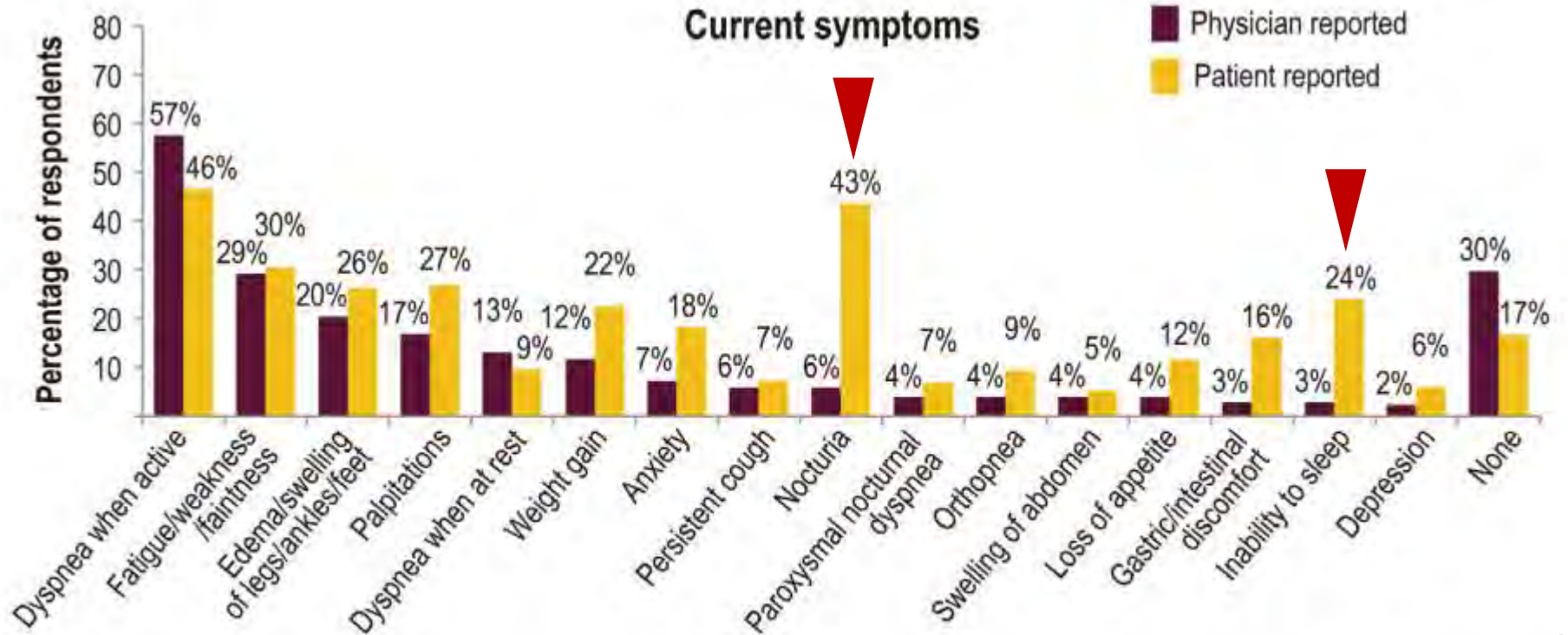


Figure 1. Physician- and patient-reported current heart failure symptoms (n=135, matched analysis of 138 physician–patient pairs).



SGLT2阻害薬の半減期？



Dapagliflozin 10mg

12.1hrs



Empagliflozin

9.88hrs



Canagliflozin

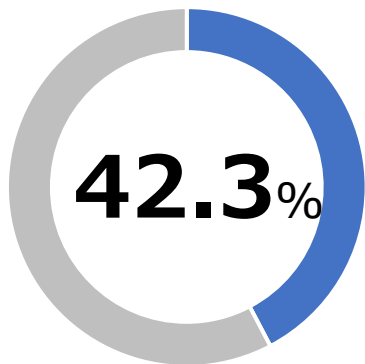
10.2hrs

演者の個人的見解

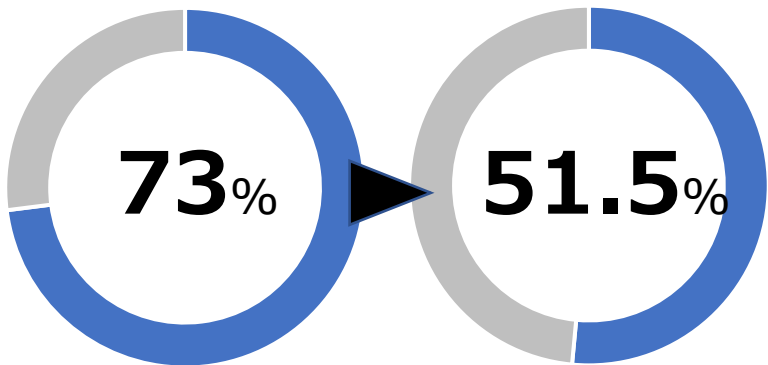


The effect of continuous positive airway pressure on nocturia in patients with obstructive sleep apnea syndrome

CPAP治療患者274名



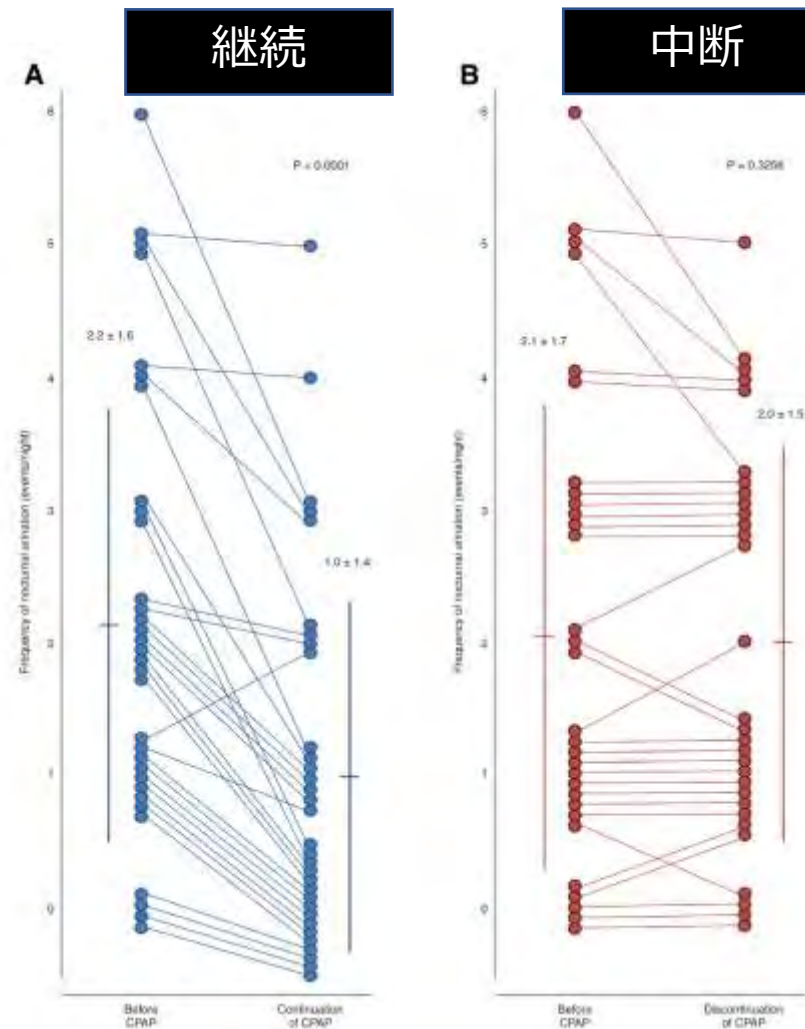
夜間排尿回数減



2回以上の
夜間頻尿例

Nocturia in Patients With Sleep-Disordered Breathing and Cardiovascular Disease

Takashi Miyazaki, MD; Sunao Kojima, MD, PhD; Megumi Yamamuro, MD, PhD; Kenji Sakamoto, MD, PhD; Yasuhiro Izumiya, MD, PhD; Kenichi Tsujita, MD, PhD; Eiichiro Yamamoto, MD, PhD; Tomoko Tanaka, MD, PhD; Koichi Kaikita, MD, PhD; Seiji Hokimoto, MD, PhD; Hisao Ogawa, MD, PhD



エビデンスに基づく

CKD

診療ガイドライン

2018

Evidence-based
Clinical Practice Guideline
for CKD
2018

第2章 生活習慣

CQ 3

CKD患者の睡眠時無呼吸症候群に対する治療は推奨されるか？

推奨 CKD患者の睡眠時無呼吸症候群に対して治療を行うよう提案する **D 2**.



High Prevalence of Obstructive Sleep Apnea and Its Association with Renal Function among Nondialysis Chronic Kidney Disease Patients in Japan: A Cross-Sectional Study

Yusuke Sakaguchi,* Tatsuya Shoji,* Hiroaki Kawabata,* Kakuya Niihata,* Akira Suzuki,* Tetsuya Kaneko,* Noriyuki Okada,† Yoshitaka Isaka,‡ Hiromi Rakugi,‡ and Yoshiharu Tsubakihara*

Clin J Am Soc Nephrol 6: 995–1000, 2011. doi: 10.2215/CJN.08670910

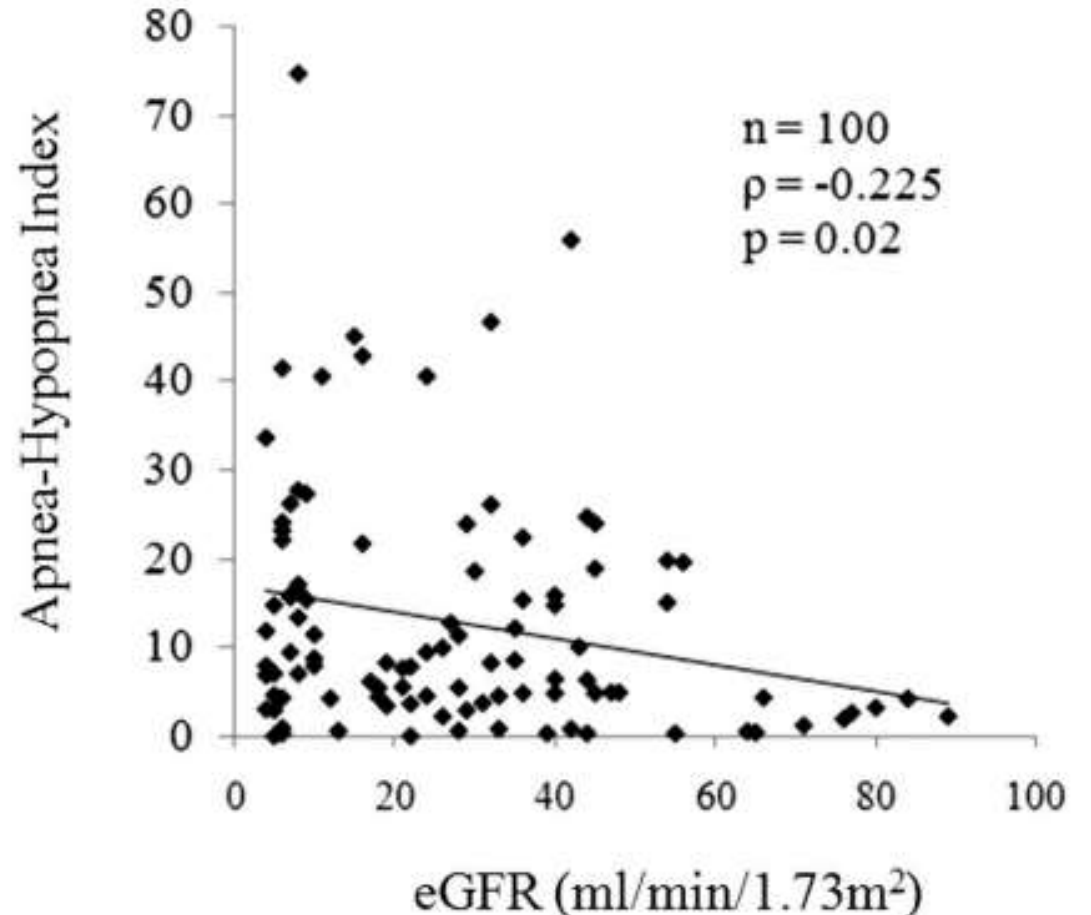
日本の非透析CKD患者

65%がOSA

eGFRの減少は、年齢、BMI、および糖尿病の調整後のOSAのオッズが42%増加

eGFRは共変量の調整後に**AHIと逆相関**

OSAの罹患率が高く、OSAのリスク上昇がGFRの低下と有意に関連



Association of Nocturnal Hypoxemia with Progression of CKD

夜間低酸素血症が腎機能を悪化

Yusuke Sakaguchi,* Tsuguru Hatta,[†] Terumasa Hayashi,[‡] Tatsuya Shoji,[‡] Akira Suzuki,[‡] Kodo Tomida,[‡] Noriyuki Okada,[§] Hiromi Rakugi,* Yoshitaka Isaka,* and Yoshiharu Tsubakihara^{||}

Clin J Am Soc Nephrol 8: 1502–1507, 2013. doi: 10.2215/CJN.11931112

腎機能
低下速度

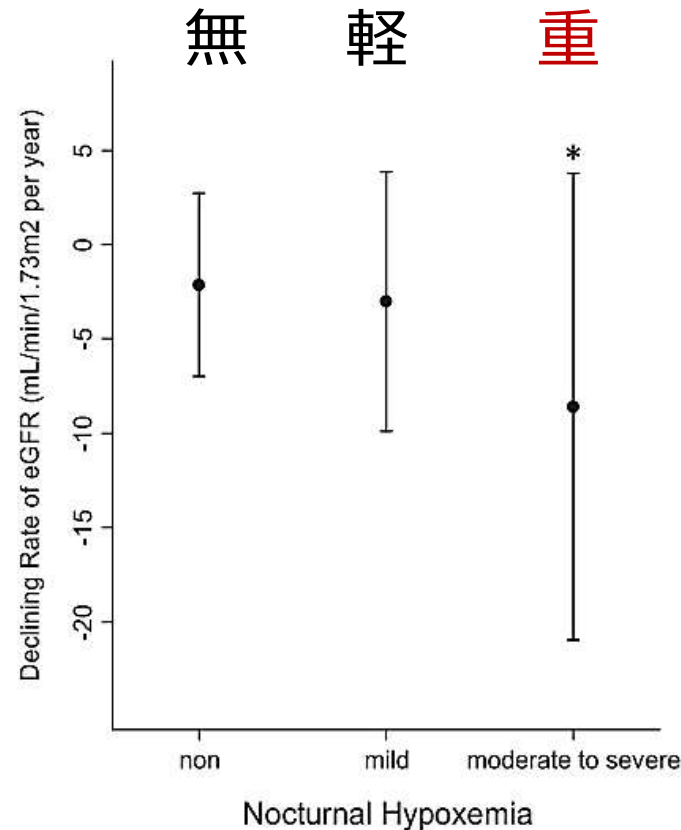


Table 2. Mixed effects multivariate linear regression model for declining rate of estimated GFR

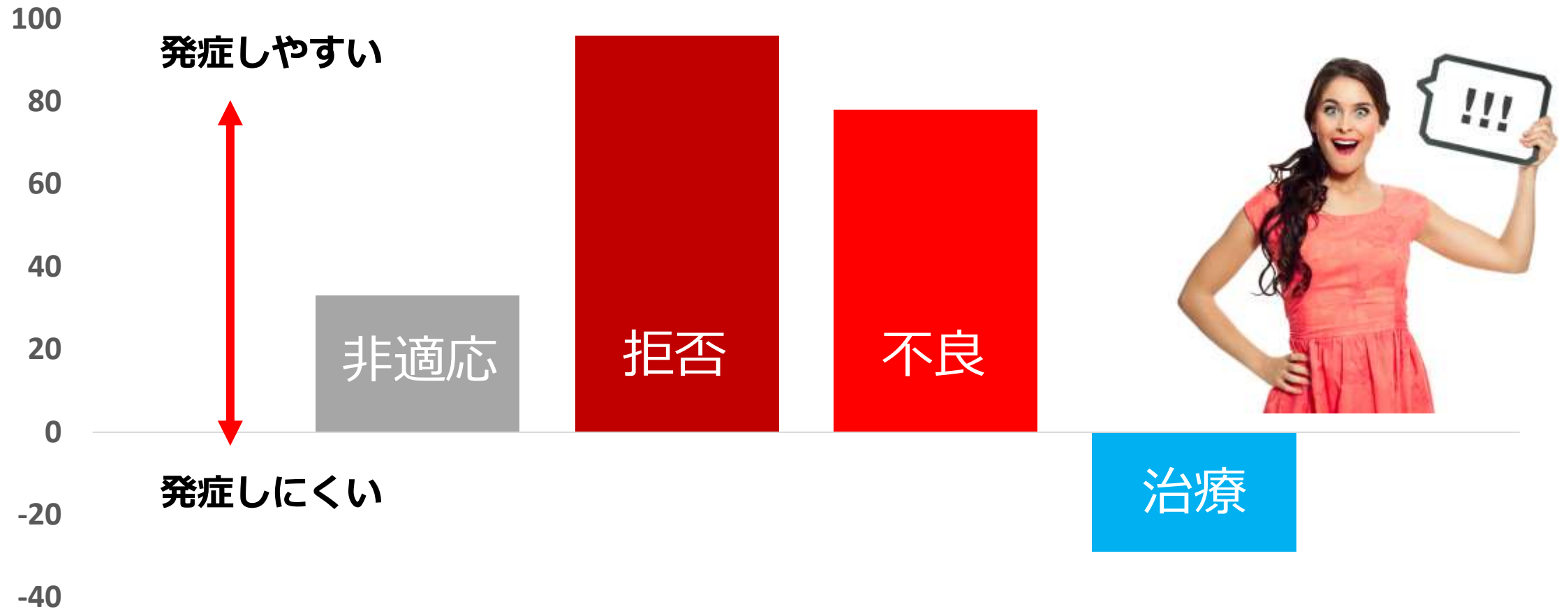
Variable	Standardized Partial Regression Coefficient	P Value
Age, yr	-0.02	0.80
Sex, man	0.06	0.42
Body mass index, kg/m ²	0.02	0.77
Type 2 diabetes mellitus	-0.09	0.23
Mean BP, mmHg	0.06	0.40
Nocturnal hypoxemia group	-0.16	0.03
Estimated GFR, ml/min per 1.73 m ²	-0.19	0.008
Urine protein, g/d	-0.40	<0.001
Serum albumin, g/dl	0.05	0.46
ACEI/ARB use	0.05	0.51
Aldosterone receptor antagonist use	0.03	0.66
Statin use	-0.08	0.26

Model adjusted for center, age, sex, estimated GFR, body mass index, mean BP, urine protein, serum albumin level, type 2 diabetic nephropathy, and medications used (ACEIs/ARBs, aldosterone receptor antagonists, and statins). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin type 2 receptor blocker.



CPAP治療によるOSAS患者の高血圧新規発症抑制

JAMA 307:2169-76,2012



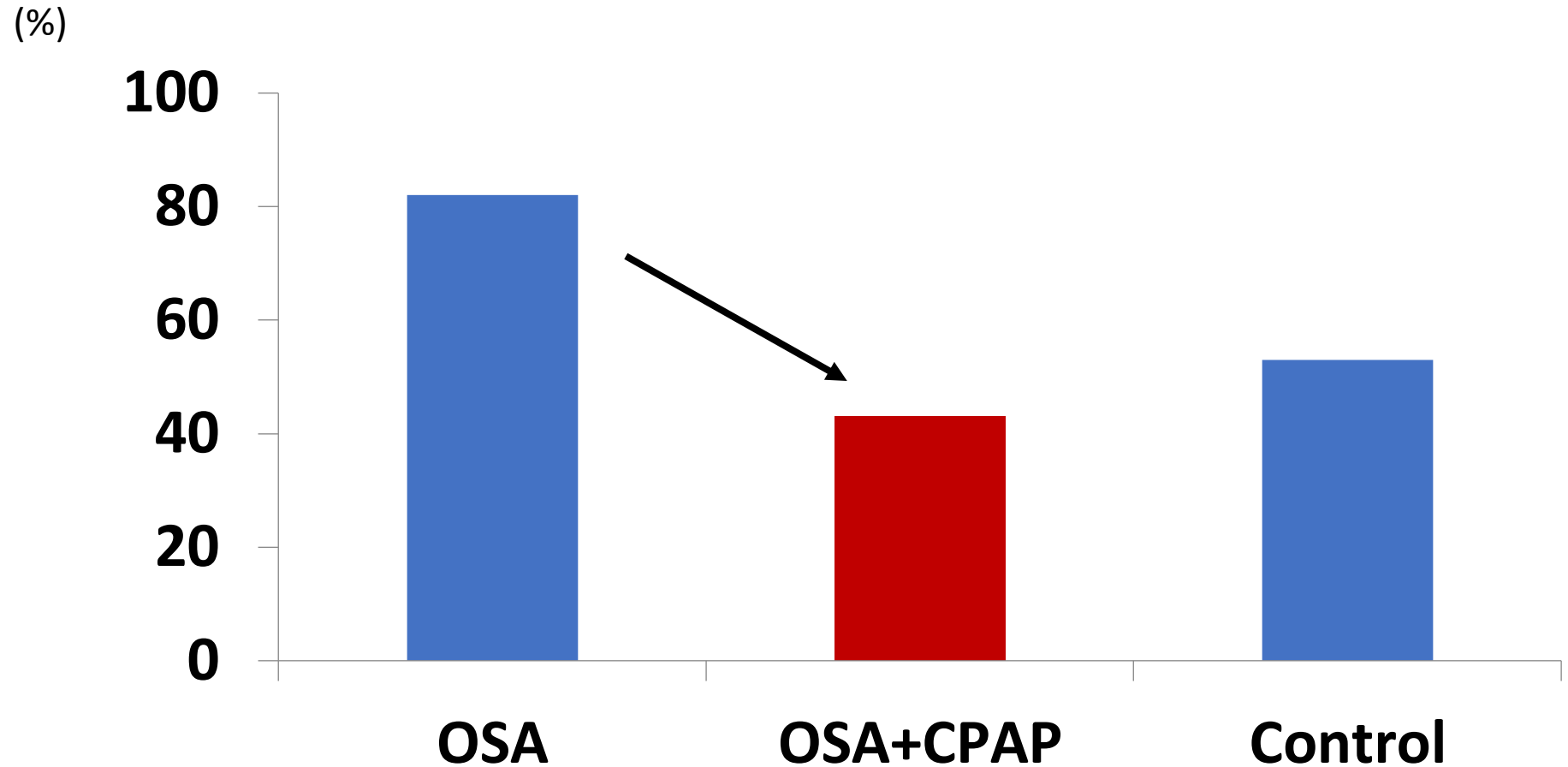
CLINICAL INVESTIGATION AND REPORTS

Obstructive Sleep Apnea and the Recurrence of Atrial Fibrillation

Ravi Kanagala, MD, Narayana S. Murali, MD, Paul A. Friedman, MD, Naser M. Ammash, MD, Bernard J. Gersh, MB ChB, DPhil, Karla V. Ballman, PhD, Abu S. M. Shamsuzzaman, MD, PhD, and Virend K. Somers, MD, PhD

OSAはAf発症に関連し
CPAPは抑制する

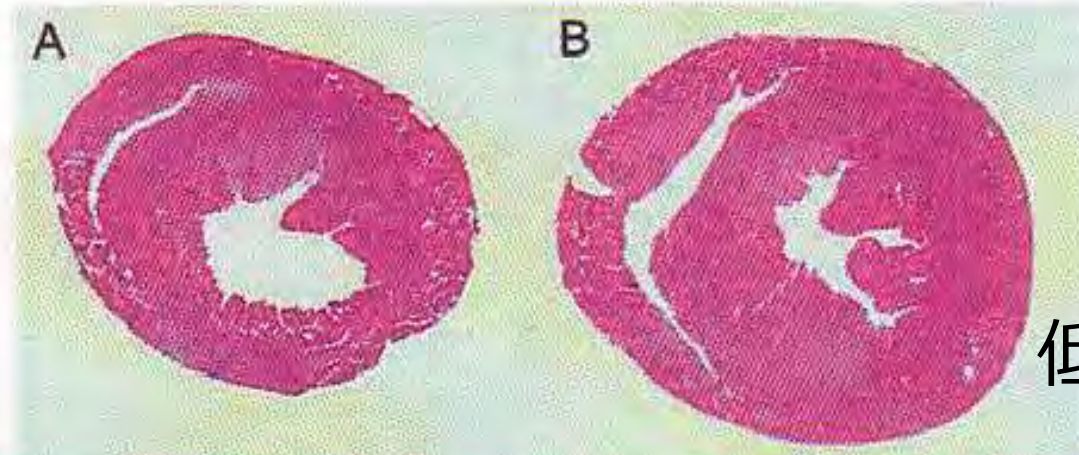
除細動後再発率



糖尿病と低酸素負荷

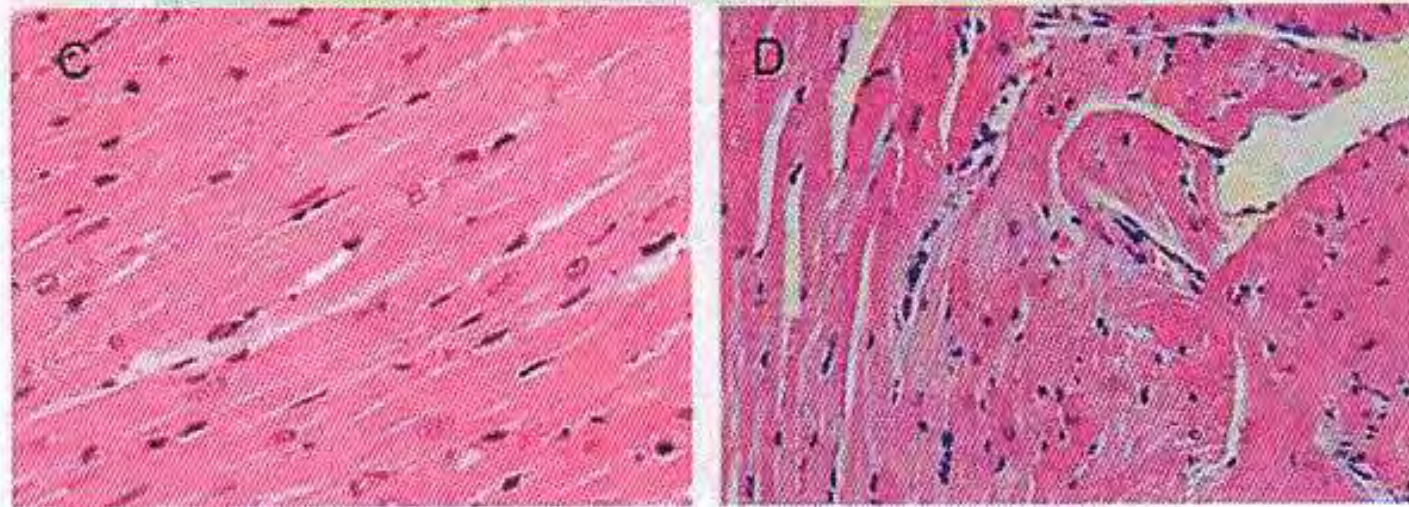
Current Cardiol Rev 2008;4:251-258.

糖尿病 + 低酸素負荷 ⇒ 心筋肥大や間質線維化が増悪



正常酸素

低酸素曝露



心臓リハ 医師の役割

医師に求められるべき技能と能力

医師自ら承認する

スタッフを活かし護る

組織構築する



システムづくり



ご興味があれば



心臓リハビリテーションの対象、
施設の運用、体制、スタッフ、
費用対効果、採算性

循環器ジャーナル67;178-186,2019



院内システムの構築



病病、病診連携の推進



演者の個人的見解



Closing



やわたメディカルセンター
YAWATA MEDICAL CENTER
病気にならないための病院



変わりたくなる「空気」をつくる



心不全再入院予防は喫緊の課題

100万円/回

Hospitalization Costs for Patients With Acute Congestive Heart Failure in Japan

Median Costs **\$8,809** per episode

Circ J. 2019 Apr 25;83(5):1025-1031

SGLT2阻害薬は心不全再入院予防に有効

THE NEW ENGLAND JOURNAL OF MEDICINE

Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure

EMPEROR-Reduced 30% ↓

THE NEW ENGLAND JOURNAL OF MEDICINE

Empagliflozin in Heart Failure with a Preserved Ejection Fraction

EMPEROR-Preserved 27% ↓

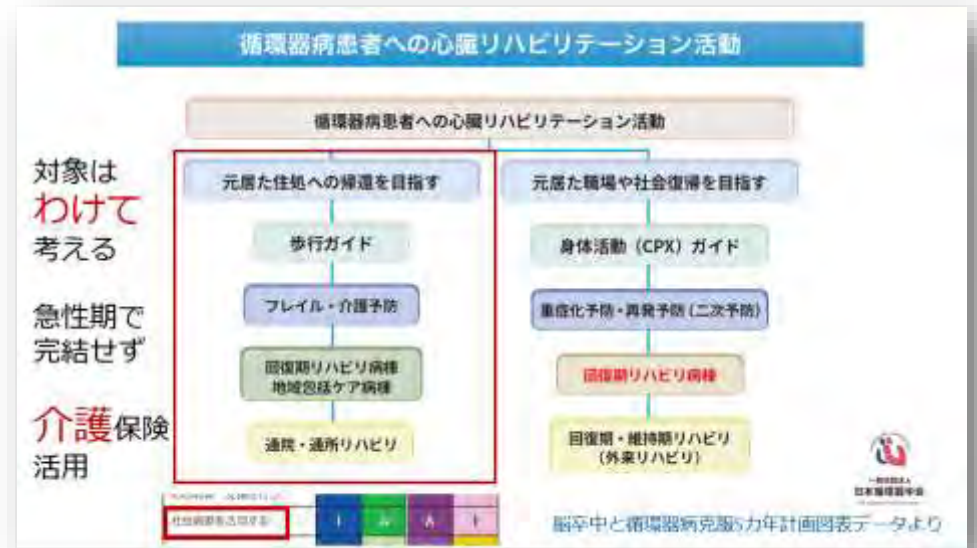
SGLT2阻害薬の多面的効果、特に腎保護

THE NEW ENGLAND JOURNAL OF MEDICINE

Efficacy of Dapagliflozin on Renal Function and Outcomes in Patients With Heart Failure With Reduced Ejection Fraction

DAPA-HFとEMPEROR-ReducedにおけるSGLT2阻害薬と偽薬での腎機能低下率

包括的地域心臓リハビリテーションの利活用



「地域ぐるみで取り組む」 JMAPスピリットそのもの

健康をサポートする

*If not **you**, then who?*

*If not **now**, then when?*





Thank you for your attention

Yawata Medical Center

