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A SELECTION OF TEN READINGS ON TOPICS RELATED TO CHRONIC DISEASE MANAGEMENT 2025

FPSC125 – SATURDAY, 18 JAN 2025 2.00pm-5.30pm
All are available as free full text

Selection of readings made by A/Prof Goh Lee Gan

READING 1 – ASSOCIATION BETWEEN BLOOD PRESSURE CONTROL AND NUTRITION EXAMINATION SURVEY

Yoon Y,[1] Son M.[2,3] PLoS One. 2024 Nov 26;19(11):e0314531. Association between blood pressure control in hypertension and urine sodium to potassium ratio: From the Korea National Health and Nutrition Examination Survey (2016-2021). PMID: 39591407.

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ABSTRACT

BACKGROUND: Hypertension (HTN) is linked to an enhanced risk of chronic kidney disease and cardiovascular disease. While sodium and potassium intake affect blood pressure (BP) control, the urine sodium-to-potassium (Na/K) ratio, which reflects dietary balance and renal regulation of these electrolytes, could be associated with BP. This study aimed to evaluate the independent association between urine Na/K and uncontrolled HTN.

METHODS: Data were collected from the Korea National Health and Nutrition Examination Survey from 2016 to 2021. A total of 5,770 participants diagnosed with HTN were enrolled in this study. Uncontrolled HTN was characterised by a systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg. Logistic regression analysis was used to assess the relationship between urine Na/K and the risk of uncontrolled HTN.

RESULTS: The urine Na/K was positively correlated with both SBP and mean arterial pressure. Higher urine Na/K was significantly associated with an increased risk of uncontrolled HTN using both continuous (odds ratio [95% confidence interval] 1.13 [1.09-1.16], P <0.01]) and across quartile values (with Q1 as a reference; Q2: 1.26 [1.06-1.49], P=0.01; Q3: 1.50 [1.27-1.78], P <0.01; Q4: 1.85 [1.55-2.17], P <0.01). The subgroup analysis also showed that higher urine Na/K was significantly related to the risk of uncontrolled HTN in the presence of proteinuria or CKD.

CONCLUSION: Urine Na/K ratio is independently associated with uncontrolled HTN in the general population and in patients with CKD. Our findings suggest that monitoring the urine Na/K could serve as an effective tool for identifying subjects at risk of uncontrolled HTN.

READING 2 – YOUNG ONSET TYPE 2 DIABETES MELLITUS ASSOCIATED WITH PROTEINURIA

Saito H,[1] Tanabe H,[1] Maimaituxun G,[1] Shimabukuro M,[1] Hirai H,[1,2] Yamaguchi S,[1,5] Higa M,[3] Tanaka K,[4] Kazama JJ,[4] Masuzaki H.[6] Young-onset type2 diabetes mellitus enhances proteinuria, but not glomerular filtration rate decline: A Japanese cohort study. J Diabetes Investig. 2024 Oct;15(10):1444-1456. PMID: 39058327.

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ABSTRACT

AIMS/INTRODUCTION: The time course of chronic kidney disease in young-onset type 2 diabetes mellitus remains unclear. We compared the trajectories of proteinuria and estimated glomerular filtration rate (eGFR) decline between young-onset (aged ≤40 years) and late-onset (aged >40 years) type 2 diabetes mellitus in a Japanese multicentre cohort.

MATERIALS AND METHODS: Participants without diabetic kidney disease were divided into two groups according to age at diagnosis: young- and late-onset. The primary endpoint was eGFR <60 mL/min/1.73 m^2, proteinuria or both. Multivariable Cox proportional hazards were calculated to estimate incidence.

RESULTS: Among 626 participants with type 2 diabetes mellitus, 78 (12.4%) had young-onset and 548 (87.6%) had late-onset diabetes. The incidence of eGFR <60 mL/min/1.73 m^2 was lower (16.7% vs 33.5%, P=0.003), but that of proteinuria was higher (46.2% vs 28.9%, P=0.002) in the young-onset type 2 diabetes mellitus group. The Kaplan-Meyer curve showed that young-onset type 2 diabetes mellitus was associated with a decreased hazard ratio (HR) for eGFR <60 mL/min/1.73 m^2 and an increased HR for proteinuria compared with late-onset type 2 diabetes mellitus. In the multivariate Cox analysis, young-onset type 2 diabetes mellitus increased the HR (95% confidence interval) of proteinuria (1.53, 95% confidence interval 1.03-2.26), but did not change the eGFR <60 mL/min/1.73 m^2 HR.

CONCLUSIONS: Young-onset type 2 diabetes mellitus has a lower HR of eGFR <60 mL/min/1.73 m^2 and an increased HR of proteinuria compared with late-onset type 2 diabetes mellitus, indicating that young-onset type 2 diabetes mellitus has a different time course for the development of proteinuria and subsequent eGFR decline.

READING 3 – RISK FACTORS FOR PROGRESSION IN PATIENTS WITH STAGE 3 CKD

Martínez-Castelao A,[1] Górriz Teruel JL,[2] D'Marco L,[3] Garrigós E,[4] Fernández-Fresnedo G,[5] Espinel Garuz E,[6] Cigarrán Guldris S,[7] Coloma JA,[8] Robles Pérez-Monteoliva NR,[9] Esteban de la Rosa JR,[10] Nieto Iglesias LJ,[11] Ortiz Arduán A,[12] Navarro-González JF.[13] PROGRESER study investigators; GEENDIAB (Spanish Group for the Study of Diabetic Nephropathy). Risk factors for progression in patients with KDOQI stage 3 Chronic Kidney Disease (PROGRESER study). Nefrologia (Engl Ed). 2024 Sep-Oct;44(5):689-699. PMID: 39510892.

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ABSTRACT

INTRODUCTION: The PROGRESER study is a multicentre, prospective, observational, 3-year follow-up study of a cohort of patients with stage 3 chronic kidney disease (CKD) from different nephrology departments of hospitals in the Spanish healthcare system. The primary study objective was to analyse risk factors for CKD progression, identifying possible differences between patients with and without diabetes mellitus (DM). The secondary objective was to analyse if the cardiovascular risk factors were also associated with CKD progression.

PATIENTS AND METHODS: A total of 462 patients (342 men and 120 women; mean age 66.5±11.5 years) were recruited from 25 participating sites in Spain. Clinical, epidemiological, and analytical data were recorded in an electronic register each six months. Biological samples were obtained and frozen for a biobank record at baseline and at 18 and 36 months.

RESULTS: The initial mean glomerular filtration rate estimated by MDRD and after that reestimated by CKD-EPI was 43.9±7.9 mL/min/1.73 m^2; and 29±6,8 mL/min/1,73 m^2 at three years. 27.3% of patients had microalbuminuria and 22.5% had macroalbuminuria. Two-thirds of the patients (66.2%) presented renal damage progression according to the study criteria (decrease of more than 15% in eGFR over the baseline value). 38.7% presented a reduction in eGFR ≥30%; 20.3% had a reduction in eGFR ≥40%; 10.4% had a reduction ≥50% and 6.9% had a reduction ≥57%. Of the 199 diabetics, 134 (67.3%) suffered renal damage progression. Of the 263 non-diabetics, 172 (65.3%) presented progression (p=0.456). 27.3% of patients had microalbuminuria and 22.5% proteinuria. The study found that CKD progression to a higher stage was not greater in diabetic compared to non-diabetic patients. Multivariate analysis revealed that the presence of arterial hypertension bordered on significance as a progression factor in non-diabetic patients (p=0.07), and that, in diabetic patients, lower calcium levels and elevated intact parathyroid hormone levels at baseline were associated with progression.

CONCLUSION: In our study, we have not found new factors for progression of renal damage, different from the yet well-known traditional factors. DM "per se" was not a differential factor for progression in relation with non-DM patients. Progression of renal damage in patients with CKD-3 KDOQI may be interpreted in a multifactorial context. The search for new biomarkers, different from traditional ones, is necessary to establish new therapeutic strategies to prevent the progression of CKD.

READING 4 – REAL WORLD EFFECTIVENESS OF EARLY INSULIN THERAPY IN NEWLY DIAGNOSED TYPE 2 DIABETES MELLITUS

Luo S,[#,1] Zheng X,[#,1] Bao W,[#,1,2] Ding Y,[1] Yue T,[1] Nie S,[3] Zhou Y,[4] Hu Y,[5] Li H,[6] Yang Q,[7] Wan Q,[8] Liu B,[9] Xu H,[10] Li G,[11] Xu G,[12] Chen C,[13] Liu H,[14] Shi Y,[15] Zha Y,[16] Kong Y,[17] Su G,[18] Tang Y,[19] Gong M,[20] Ji L,[21] Hou FF,[22] Weng J.[23] Real-world effectiveness of early insulin therapy on the incidence of cardiovascular events in newly diagnosed type 2 diabetes. Signal Transduct Target Ther. 2024 Jun 6;9(1):154. PMID: 38844816.

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ABSTRACT

Early insulin therapy is capable to achieve glycaemic control and restore β-cell function in newly diagnosed type 2 diabetes (T2D), but its effect on cardiovascular outcomes in these patients remains unclear.

In this nationwide real-world study, we analysed electronic health record data from 19 medical centres across China between 1 January 2000 and 26 May 2022. We included 5,424 eligible patients (mean age 56 years, 2,176 women/3,248 men) who were diagnosed with T2D within six months and did not have prior cardiovascular disease. Multivariable Cox regression models were used to estimate the associations of early insulin therapy (defined as the first-line therapy for at least two weeks in newly diagnosed T2D patients) with the incidence of major cardiovascular events including coronary heart disease (CHD), stroke, and hospitalisation for heart failure (HF).

During 17,158 persons years of observation, we documented 834 incident CHD cases, 719 stroke cases, and 230 hospitalised cases for HF. Newly diagnosed T2D patients who received early insulin therapy, compared with those who did not receive such treatment, had 31% lower risk of incident stroke, and 28% lower risk of hospitalisation for HF. No significant difference in the risk of CHD was observed. We found similar results when repeating the aforesaid analysis in a propensity-score matched population of 4,578 patients and with inverse probability of treatment weighting models.

These findings suggest that early insulin therapy in newly diagnosed T2D may have cardiovascular benefits by reducing the risk of incident stroke and hospitalisation for HF.

READING 5 – REAL-WORLD OUTCOMES OF INDIVIDUALISED TARGETED THERAPY WITH INSULIN GLARGINE IN INSULIN-NAÏVE TYPE 2 DIABETES MELLITUS

Hong EG,[1] Min KW,[2] Lim JS,[3] Ahn KJ,[4] Ahn CW,[5] Yu JM,[6] Kim HS,[7] Kim HJ,[8] Kim W,[9] Kim DH,[9] Jang HC.[10] Real-World Outcomes of Individualized Targeted Therapy with Insulin Glargine 300 Units/mL in Insulin-Naïve Korean People with Type 2 Diabetes: TOBE Study. Adv Ther. 2024 May;41(5):1967-1982. PMID: 38512540.

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ABSTRACT
INTRODUCTION: The TOujeo BEyond glucose control (TOBE) study evaluated clinical outcomes with insulin glargine 300 units/mL (Gla-300) in insulin-naïve Korean people with type 2 diabetes mellitus (T2DM) in a real-world setting.

METHODS: This 24-week, prospective, non-interventional, multicentre, open-label, single-arm, observational study included adults aged ≥20 years with T2DM suboptimally controlled with oral hypoglycaemic agents and/or glucagon-like peptide 1 receptor agonists who require basal insulin. Eligible participants were assigned to either general target glycated haemoglobin (HbA1c <7%) or individualised target groups as per physician's discretion considering guidelines and participants' characteristics. The primary endpoint was the proportion of participants achieving the HbA1c target (individualised or general) at 24 weeks.

RESULTS: Among 369 participants, 19.5% (72/369) of participants achieved the HbA1c target at week 24; 37.5% (33/88) in the individualised and 13.9% (39/281) in the general target group. In both target groups, similar reductions in fasting plasma glucose and body weight were observed, with low incidence of hypoglycaemia, and T2DM duration was significantly shorter in participants who did versus those who did not achieve the target HbA1c (individualised target group: 9.6±8.0 versus 13.1±8.4 years, P=0.0454; general target group: 10.2±8.6 versus 12.8±7.4 years, P=0.0378).

CONCLUSIONS: This study showed that initiation of insulin therapy with Gla-300 in people with T2DM using an individualised approach is more effective in achieving an HbA1c target. Moreover, earlier initiation of insulin therapy in people with suboptimally controlled T2DM may increase the success rate of glycaemic control. A graphical abstract is available with this article.

READING 6 – INTERVENTIONS TO PREVENT OBESITY IN CHILDREN 12-18 YEARS OLD

Spiga F,[1] Tomlinson E,[1] Davies AL,[1] Breheny K,[1] Moore TH,[1,2] Dawson S,[1,2] Savović J,[1,2] Higgins JP,[1,2] Hodder RK,[3,4] Wolfenden L,[3,4] Summerbell CD.[5,6] Interventions to prevent obesity in children aged 12 to 18 years old. Cochrane Database Syst Rev. 2024 May 20;5(5):CD015330. PMID:38763518.

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ABSTRACT
BACKGROUND: Prevention of obesity in adolescents is an international public health priority. The prevalence of overweight and obesity is over 25% in North and South America, Australia, most of Europe, and the Gulf region. Interventions that aim to prevent obesity involve strategies that promote healthy diets or "activity" levels (physical activity, sedentary behaviour, and/or sleep) or both, and work by reducing energy intake and/or increasing energy expenditure, respectively. There is uncertainty over which approaches are more effective, and numerous new studies have been published over the last five years since the previous version of this Cochrane Review.

OBJECTIVES: To assess the effects of interventions that aim to prevent obesity in adolescents by modifying dietary intake or "activity" levels, or a combination of both, on changes in BMI, zBMI score, and serious adverse events.

SEARCH METHODS: We used standard, extensive Cochrane search methods. The latest search date was February 2023.

SELECTION CRITERIA: Randomised controlled trials in adolescents (mean age 12 years and above but less than 19 years), comparing diet or "activity" interventions (or both) to prevent obesity with no intervention, usual care, or with another eligible intervention, in any setting. Studies had to measure outcomes at a minimum of 12 weeks post-baseline. We excluded interventions designed primarily to improve sporting performance.

DATA COLLECTION AND ANALYSIS: We used standard Cochrane methods. Our outcomes were BMI, zBMI score, and serious adverse events, assessed at short- (12 weeks to <9 months from baseline), medium- (9 months to <15 months), and long-term (≥15 months) follow-up. We used GRADE to assess the certainty of the evidence for each outcome.

MAIN RESULTS: This review includes 74 studies (83,407 participants); 54 studies (46,358 participants) were included in meta-analyses. Sixty studies were based in high-income countries. The main setting for intervention delivery was schools (57 studies), followed by home (nine studies), the community (five studies), and a primary care setting (three studies). Fifty-one interventions were implemented for less than nine months; the shortest was conducted over one visit and the longest over 28 months. Sixty-two studies declared non-industry funding; five were funded in part by industry.

DIETARY INTERVENTIONS VERSUS CONTROL: The evidence is very uncertain about the effects of dietary interventions on body mass index (BMI) at short-term follow-up (mean difference (MD) -0.18, 95% confidence interval (CI) -0.41 to 0.06; three studies, 605 participants), medium-term follow-up (MD -0.65, 95% CI -1.18 to -0.11; three studies, 900 participants), and standardised BMI (zBMI) at long-term follow-up (MD -0.14, 95% CI -0.38 to 0.10; two studies, 1,089 participants); all very low-certainty evidence. Compared with control, dietary interventions may have little to no effect on BMI at long-term follow-up (MD -0.30, 95% CI -1.67 to 1.07; one study, 44 participants); zBMI at short-term (MD -0.06, 95% CI -0.12 to 0.01; 5 studies, 3,154 participants); and zBMI at medium-term (MD 0.02, 95% CI -0.17 to 0.21; one study, 112 participants) follow-up; all low-certainty evidence. Dietary interventions may have little to no effect on serious adverse events (two studies, 377 participants; low-certainty evidence).

ACTIVITY INTERVENTIONS VERSUS CONTROL: Compared with control, activity interventions do not reduce BMI at short-term follow-up (MD -0.64, 95% CI -1.86 to 0.58; six studies, 1,780 participants; low-certainty evidence) and probably do not reduce zBMI at medium- (MD 0, 95% CI -0.04 to 0.05; six studies, 5335 participants) or long-term (MD -0.05, 95% CI -0.12 to 0.02; 1 study, 985 participants) follow-up; both moderate-certainty evidence. Activity interventions do not reduce zBMI at short-term follow-up (MD 0.02, 95% CI -0.01 to 0.05; seven studies, 4,718 participants; high-certainty evidence), but may reduce BMI slightly at medium-term (MD -0.32, 95% CI -0.53 to -0.11; three studies, 2143 participants) and long-term (MD -0.28, 95% CI -0.51 to -0.05; one study, 985 participants) follow-up; both low-certainty evidence. Seven studies (5,428 participants; low-certainty evidence) reported data on serious adverse events: two reported injuries relating to the exercise component of the intervention and five reported no effect of intervention on reported serious adverse events.

DIETARY AND ACTIVITY INTERVENTIONS VERSUS CONTROL: Dietary and activity interventions, compared with control, do not reduce BMI at short-term follow-up (MD 0.03, 95% CI -0.07 to 0.13; 11 studies, 3,429 participants; high-certainty evidence), and probably do not reduce BMI at medium-term (MD 0.01, 95% CI -0.09 to 0.11; eight studies, 5,612 participants; moderate-certainty evidence) or long-term (MD 0.06, 95% CI -0.04 to 0.16; six studies, 8,736 participants; moderate-certainty evidence) follow-up. They may have little to no effect on zBMI in the short term, but the evidence is very uncertain (MD -0.09, 95% CI -0.2 to 0.02; three studies, 515 participants; very low-certainty evidence), and they may not reduce zBMI at medium-term (MD -0.05, 95% CI -0.1 to 0.01; six studies, 3,511 participants; low-certainty evidence) or long-term (MD -0.02, 95% CI -0.05 to 0.01; seven studies, 8,430 participants; low-certainty evidence) follow-up. Four studies (2,394 participants) reported data on serious adverse events (very low-certainty evidence): one reported an increase in weight concern in a few adolescents and three reported no effect.

CONCLUSIONS: The evidence demonstrates that dietary interventions may have little to no effect on obesity in adolescents. There is low-certainty evidence that activity interventions may have a small beneficial effect on BMI at medium- and long-term follow-up. Diet plus activity interventions may result in little to no difference. Importantly, this updated review also suggests that interventions to prevent obesity in this age group may result in little to no difference in serious adverse effects. Limitations of the evidence include inconsistent results across studies, lack of methodological rigour in some studies, and small sample sizes. Further research is justified to investigate the effects of diet and activity interventions to prevent childhood obesity in community settings, and in young people with disabilities, since very few ongoing studies are likely to address these. Further randomised trials to address the remaining uncertainty about the

effects of diet, activity interventions, or both, to prevent childhood obesity in schools (ideally with zBMI as the measured outcome) would need to have larger samples.

READING 7 – HIGHER ADHERENCE TO THE MEDITERRANEAN DIET IS ASSOCIATED WITH A LOWER RISK OF STEATOTIC, ALCOHOL-RELATED, AND METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE: A RETROSPECTIVE ANALYSIS

Lee JY,[1] Lee JW,[1,5] Kim S,[2] Lee Y,[3] Kwon YJ.[4] Higher Adherence to the Mediterranean Diet Is Associated with a Lower Risk of Steatotic, Alcohol-Related, and Metabolic Dysfunction-Associated Steatotic Liver Disease: A Retrospective Analysis. Nutrients. 2024 Oct 19;16(20):3551. PMID: 39458545.

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ABSTRACT

BACKGROUND AND AIMS: Metabolic liver disease is associated with obesity, insulin resistance, cardiovascular disease, and metabolic disorders. A Mediterranean diet (MD), known for its anti-inflammatory and antioxidant properties, is effective in managing various chronic diseases, including liver diseases. This study aimed to explore the influence of adherence to the MD on the risk of chronic metabolic diseases, including steatotic liver disease (SLD), metabolic dysfunction-associated steatotic liver disease (MASLD), and alcohol-related liver diseases (ALDs).

METHODS: This retrospective cohort study analysed 5,395 individuals from a single centre between 2020 and 2022, grouped by adherence to the MD using the Korean Mediterranean Diet Adherence Score (K-MEDAS). MASLD score, ALD, and cardiovascular risk factors were also assessed. Statistical analyses were performed using 1:1 exact matching and multiple regression to compare the less adherent (K-MEDAS 0-7) and highly adherent (K-MEDAS 8-13) groups.

RESULTS: Adjusting for confounding variables, high adherence to the MD was significantly associated with lower rates of SLD (odds ratio [OR] 0.818, 95% confidence interval [CI] 0.700-0.957, p=0.012), MASLD (OR 0.839, 95% CI 0.714-0.986, p=0.033), and ALD (OR 0.677, 95% CI 0.671-0.683, p<0.001). Post-propensity score matching analysis revealed that the highly adherent group exhibited significantly lower triglyceride levels, triglyceride and glucose index, atherogenic Index of Plasma, and Framingham risk scores than the less adherent group.

CONCLUSIONS: Good adherence to the MD considerably reduces the risk of SLD, MASLD, and ALD, underscoring its protective effects and potential to prevent metabolic liver diseases and their complications.

READING 8 – THE EFFECT OF WEIGHT LOSS THROUGH LIFESTYLE INTERVENTIONS IN PATIENTS WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION – A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS

Lee VYJ,[1] Houston L,[2] Barraclough JY,[2] Perkovic A,[3] Sweeting A,[4] Yu J,[5] Fletcher RA,[6] Arnott C.[7] The Effect of Weight Loss Through Lifestyle Interventions in Patients With Heart Failure With Preserved Ejection Fraction-A Systematic Review and Meta-Analysis of Randomised Controlled Trials. Heart Lung Circ. 2024 Feb;33(2):197-208. PMID: 38320881

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ABSTRACT

BACKGROUND: Heart failure with preserved ejection fraction (HFpEF) accounts for >50% of heart failure cases and is associated with significant morbidity and health system burden. To date, there have been limited treatment options proven to improve outcomes in these patients, with sodium glucose co-transporter 2 (SGLT2) inhibitors the first class of drug to demonstrate significant clinical benefits, including reductions in heart failure hospitalisation. Obesity is associated with all forms of heart failure and has been linked with worse clinical outcomes. Numerous reviews support the benefits of weight loss in heart failure, more specifically in patients with heart failure with reduced ejection fraction. However, the evidence in HFpEF patients is less clear. With limited pharmacotherapy options and growing support for weight loss in patients with HFpEF, this systematic review and meta-analysis aims to examine the effects of lifestyle interventions on weight loss and other health outcomes in patients with HFpEF.

METHODS: Web of Science, Embase, Scopus, and PubMed databases were searched to identify relevant studies up to February 2023. Included studies were randomised controlled trials (with a duration of four weeks or more) of lifestyle interventions conducted in adults with HFpEF that reported weight loss. Outcomes of interest were body weight, body mass index (BMI), blood pressure (systolic and diastolic), aerobic capacity (6-minute walk distance), New York Heart Association (NYHA) Functional Classification, self-reported health quality of life (Minnesota Living with Heart Failure Questionnaire; MLHFQ), and N-terminal pro B-Type Natriuretic Peptide (NT-proBNP) levels. Review Manager software was used to conduct random effect meta-analyses, forest plots were generated for each outcome, and between-study heterogeneity was estimated using the I2 test statistic. Risk-of-bias assessment used the Cochrane risk-of-bias tool, and the certainty of the evidence was assessed using GRADE.

RESULTS: From 2,282 records identified, six studies with a total of 375 participants, between three to six months in duration, were included in this systematic review and meta-analysis. Lifestyle interventions consisted of diet only, exercise only, combination of diet and exercise, and education and exercise. Over a mean follow-up of 4.5 months, pooled effects of the interventions were associated with a reduction in body weight of >5 kg (weight mean difference (WMD): -5.30 kg; 95% CI: -8.72 to -1.87; p=0.002), and a reduction in resting systolic (WMD: -2.98 mmHg; 95% CI: -4.20 to -1.76; p<0.001) and diastolic blood pressure (WMD: -4.51 mmHg; 95% CI: -8.39 to -0.64; p=0.02) compared with those who received usual care. Interventions also improved 6-minute walk distance (WMD: 43.63 m; 95% CI: 22.28 to 64.97; p<0.001), NYHA class (WMD: -0.54; 95% CI: -0.75 to -0.33; p<0.001), and MLHFQ score (WMD: -17.77; 95% CL: -19.00 to -16.53; p<0.001).

CONCLUSION: In patients with HFpEF, lifestyle intervention was associated with a significant reduction in body weight and had favourable effects on blood pressure, aerobic capacity, NYHA class, and health-related quality of life. Further research is needed in this population to examine the feasibility and durability of weight loss interventions and to examine the potential impact on hard clinical endpoints.

READING 9 – AGE-STRATIFIED PROFILES AND OUTCOMES OF PATIENTS WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION

Yamanaka S,[1] Nochioka K,[1] Hayashi H,[1] Shiroto T,[1] Takahashi J,[1] Yasuda S,[1] Shimokawa H,[1,3] Miyata S[2]; CHART-2 Investigators. Age-stratified profiles and outcomes of patients with heart failure with preserved ejection fraction. ESC Heart Fail. 2024 Aug;11(4):2223-2233. PMID: 38627993.

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ABSTRACT

AIMS: This study aimed to elucidate age-stratified clinical profiles and outcomes in patients with heart failure (HF) with preserved left ventricular ejection fraction (LVEF) (HFpEF).

METHODS AND RESULTS: The Chronic Heart Failure Registry and Analysis in the Tohoku District-2 (CHART-2) Study included 2,824 consecutive HFpEF patients with LVEF ≥50% (mean age 69.0±12.3 years; 67.7% male) with a median follow-up of 9.8 years. We stratified them into five age groups: ≤54 (N=349, 12.4%), 55-64 (N=529, 18.7%), 65-74 (N=891, 31.6%), 75-84 (N=853, 30.2%), and ≥85 years (N=202, 7.2%), and we categorised these age groups into younger (≤64 years) and older (≥65 years) groups. We compared the clinical profiles and outcomes of HFpEF patients across age groups. Younger HFpEF groups exhibited a male predominance, elevated body mass index (BMI), and poorly controlled diabetes (haemoglobin A1c>7.0%). Older HFpEF groups were more likely to be female with multiple comorbidities, including coronary artery disease, hypertension, renal impairment, and atrial fibrillation. The positive association between elevated BMI and HFpEF was more pronounced with lower classes of age from ≥85 to ≤54 years, especially in males. With higher classes of age from ≤54 to ≥85 years, mortality rates increased, and HF death became proportionally more prevalent (Ptrend<0.001), whereas sudden cardiac death (SCD) exhibited the opposite trend (Ptrend=0.002). Poorly controlled diabetes emerged as the only predictor of SCD in the younger groups (adjusted hazard ratio 4.26; 95% confidence interval 1.45-12.5; P=0.008). Multiple comorbidities were significantly associated with an increased risk of HF-related mortality in the older groups.

CONCLUSIONS: Younger HFpEF patients (≤64 years) exhibit a male predominance, elevated BMI, and poorly controlled diabetes, highlighting the importance of glycaemic control in reducing SCD risk. Older HFpEF patients (≥65 years) are more likely to be female, with multiple comorbidities linked to an increased risk of HF-related mortality. These findings underscore the need for physicians to recognise age-related, distinct HFpEF phenotypes for personalised patient management.

READING 10 – THE EFFECTS OF DAPAGLIFLOZIN IN A REAL-WORLD POPULATION OF HFREF PATIENTS WITH DIFFERENT HEMODYNAMIC PROFILES: WORSE IS BETTER?

Loria F,[1] Di Fonzo R,[1] Izzo C,[1] Visco V,[1] Vecchione C,[1,16] Mone P,[2-4] Santulli G,[3,15] Rispoli A,[5] Campanile A,[5] Virtuoso N,[5] Masarone D,[6] Falco L,[6] Mancusi C,[7] Correale M,[8] Vitullo A,[8] Granatiero M,[8] Mazzeo P,[9] Stabile E,[9] Mercurio V,[10] Fiore F,[10] Di Sarro E,[10] Tocchetti CG,[10,12-14] Bonanno S,[11] Dattilo G,[11] Ciccarelli M.[17] The effects of Dapagliflozin in a real-world population of HFrEF patients with different hemodynamic profiles: worse is better. Cardiovasc Diabetol. 2024 Nov 22;23(1):423. PMID: 39578847.

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ABSTRACT

BACKGROUND: Sodium-Glucose Cotransporter-2 inhibitors (SGLT2i) represent a deep revolution of the therapeutic approach to heart failure (HF), preventing its insurgence but also improving the management of the disease and slowing its natural progression. To date, few studies have explored the effectiveness of SGLT2i and, in particular, Dapagliflozin in a real-world population. Therefore, in this observational prospective study, we evaluated Dapagliflozin's effectiveness in a real-world HF population categorised in the different hemodynamic profiles.

METHODS: From January 2022 to June 2023, we enrolled 240 patients with chronic HF and reduced ejection fraction (HFrEF) on optimal medical therapy, according to 2021 ESC guidelines, that added treatment with Dapagliflozin from the HF Clinics of six Italian University Hospitals. Clinical, biochemical, and echocardiographic parameters were collected before and after six months of Dapagliflozin introduction. Moreover, the HFrEF population was classified according to hemodynamic profiles (A: SV ≥35 ml/m^2; E/e' <15; B: SV ≥35 ml/m^2; E/e' ≥15; C: SV <35 ml/m^2; E/e' <15; D: SV <35 ml/m^2; E/e' ≥15). Then, we compared the Dapagliflozin population with two retrospective HF cohorts, hereinafter referred to as Guide Line 2012 (GL 2012) group and Guide Line 2016 (GL 2016) group, in accordance with the HF ESC guidelines in force at the time of patient's enrolment. Precisely, we evaluated the changes to baseline in clinical, functional, biochemical, and echocardiographic parameters and compared them to the GL 2012 and GL 2016 groups.

RESULTS: Dapagliflozin population (67.18±11.11 years) showed a significant improvement in the echocardiographic and functional parameters (left ventricular ejection fraction [LVEF], LV end-diastolic volume [LVEDV], LVEDV index, stroke volume index [SVi], left atrium volume index [LAVi], filling pressure [E/e' ratio], tricuspid annular plane systolic excursion [TAPSE], tricuspid annular S' velocity [RVs'], fractional area change [FAC], inferior vena cava [IVC diameter], pulmonary artery systolic pressure [sPAP], NYHA class, and quality of life) compared to baseline. In particular, TAPSE and right ventricle diameter (RVD1) ameliorate in congestive profiles (B and D); accordingly, the furosemide dose significantly decreased in these profiles. Comparing the three populations, the analysis of echocardiographic parameters (baseline vs follow-up) highlighted a significant decrease of sPAP in the Dapagliflozin population ($p<0.05$), while no changes were

recorded in the GL 2012 and GL 2016 population. Moreover, at the baseline evaluation, the GL 2012 and 2016 groups needed a higher significant dose of furosemide compared to Dapagliflozin group. Finally, Dapagliflozin patients had significantly fewer rehospitalizations (1.25%) compared with the other two groups (GL 2012 18.89%, p 0.0097; GL 2016 15.32%, p 0.0497).

CONCLUSIONS: We demonstrate that Dapagliflozin is rapidly effective in an HFrEF real-world population; furthermore, the more significant effect is recorded in HFrEF patients with a congestive profile (B and D), supporting the introduction of Dapagliflozin in patients with a congestive profile and a worse prognosis. In conclusion, our data suggest evaluating the patient's hemodynamic state beyond LVEF in HFrEF.