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

Some available as free full-text and some requiring payment

Selection of readings made by A/Prof Goh Lee Gan

READING 1 – SGLT2 INHIBITOR ON RENAL FUNCTION IN T2DM PATIENTS

Feng C(1), Wu M(1), Chen Z(1), Yu X(1), Nie Z(1), Zhao Y(1), Bao B(2).. Effect of SGLT2 inhibitor on renal function in patients with type 2 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials. Int Urol Nephrol. 2019 Apr;51(4):655-669.

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ABSTRACT

OBJECTIVE: This study summarizes the evidence from randomized controlled trials (RCTs) to assess the effects of SGLT2 inhibitors on renal function and albuminuria in patients with type 2 diabetes.

MATERIALS/METHODS: We searched PubMed, Web of Science, Cochrane Library and EMBASE for reports published up to March 2018 and included RCTs reporting estimated glomerular filtration rate (eGFR) and/or urine albumin/creatinine ratio (UACR) changes. Data extraction and assessment of research quality based on Cochrane risk biasing tools. Data were calculated to represent the standardized mean difference (SMD) for each study, and the SMDs with 95% confidence intervals (CIs) were pooled using a random effects model.

RESULTS: Fifty-one studies were included that evaluated eGFR levels, and 17 studies were included that evaluated UACR levels. A meta-analysis showed that SGLT2 inhibitors had no significant effect on eGFR levels (SMD -0.02, 95% CI -0.06, 0.03, p=0.45), and eGFR reduction was observed in the subsets of the duration of the trial 12<duration≤26 weeks (SMD -0.08, 95% CI -0.13, -0.02, p=0.005) and mean baseline eGFR<60 ml/min per 1.73 square meters (SMD -0.22, 95% CI -0.37, -0.07, p=0.004). We found that SGLT2 inhibitors reduced UACR levels in patients with type 2 diabetes (SMD -0.11, 95% CI -0.17, -0.05, p=0.0001). Compared with monotherapy, the combination with other hypoglycemic agents can reduce albuminuria levels (SMD -0.13, 95% CI -0.19, -0.06, p<0.0001).

CONCLUSIONS: The effect of SGLT2 inhibitor on eGFR in patients with T2DM was not statistically significant, but it was effective in reducing albuminuria levels.

READING 2 – COMPARING EFFECTS OF DPP4 INHIBITORS AND SULPHONYLUREAS ON ALBUMINURIA IN T2DM PATIENTS

Cheng PC(1), Hsu SR(2), Kuo JF(3), Cheng YC(4), Liu YH(5), Tu ST(6). Comparing the Effect of Dipeptidyl-Peptidase 4 Inhibitors and Sulfonylureas on Albuminuria in Patients with Newly Diagnosed Type 2 Diabetes Mellitus: A Prospective Open-Label Study. J Clin Med. 2019 Oct 17;8(10). pii: E1715.

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ABSTRACT

Diabetic kidney disease (DKD) leads to substantial morbidity in patients with type 2 diabetes mellitus (T2DM). Evidence suggests that antidiabetic drug dipeptidyl-peptidase 4 (DPP-4) inhibitors may be able to attenuate albuminuria, whereas the influence of sulfonylureas on albuminuria remains unclear.

This prospective open-label study investigated the effect of DPP-4 inhibitors and sulfonylureas on urinary albumin excretion, which is a marker of renal microvascular abnormality. A total of 101 participants with newly diagnosed T2DM were enrolled. In addition to metformin therapy, 45 patients were assigned to receive DPP-4 inhibitors and 56 to receive sulfonylureas.

Urinary albumin-to-creatinine ratio (ACR) was significantly reduced in recipients of DPP-4 inhibitors after 24 weeks (29.2 μg/mg creatinine vs. 14.9 μg/mg creatinine, $P < 0.001$), whereas urinary ACR was not significantly changed by sulfonylureas (39.9 μg/mg creatinine vs. 43.2 μg/mg creatinine, $P = 0.641$). The effect on albuminuria occurred even though both treatment groups had a similar change in serum glycated hemoglobin A1c (-1.87 % vs.-2.40 %, $P = 0.250$).

Therefore, in diabetic patients the addition of DPP-4 inhibitors lowered urinary albumin excretion compared to sulfonylureas, and attenuation of albuminuria may be a consideration when choosing between antidiabetic medications.

READING 3 – READING 3 – T2DM OUTPATIENT INSULIN MANAGEMENT

Howard-Thompson A(1), Khan M(2), Jones M(3), George CM(2). Type 2 Diabetes Mellitus: Outpatient Insulin Management. Am Fam Physician. 2018 Jan 1;97(1):29-37.

PubMed PMID: 29365240: Free full text

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ABSTRACT

In patients with type 2 diabetes mellitus, insulin may be used to augment therapy with oral glycemic medications or as insulin replacement therapy.

The American Diabetes Association suggests the use of long-acting (basal) insulin to augment therapy with one or two oral agents or one oral agent plus a glucagon-like peptide 1 receptor agonist when the A1C level is 9% or more, especially if the patient has symptoms of hyperglycemia or catabolism.

Insulin regimens should be adjusted every three or four days until targets of self-monitored blood glucose levels are reached. A fasting and premeal blood glucose goal of 80 to 130 mg per dL and a two-hour postprandial goal of less than 180 mg per dL are recommended. Insulin use is associated with hypoglycemia and weight gain. Insulin analogues are as effective as human insulin at lowering A1C levels with lower risk of hypoglycemia, but they have significantly higher cost. Patients with one or more episodes of severe hypoglycemia (i.e., requiring assistance from others for treatment) may benefit from a short-term relaxation of glycemic targets. Several new insulin formulations have been approved recently that are associated with less risk of hypoglycemia compared with older formulations.

The goals of therapy should be individualized based on many factors, including age, life expectancy, comorbid conditions, duration of diabetes, risk of hypoglycemia, cost, patient motivation, and quality of life.

READING 4 – EXERCISE PRESCRIPTION FOR WEIGHT MANAGEMENT IN OBESE ADULTS AT RISK FOR OSTEOARTHRITIS

Barrow DR(1), Abbate LM(2)(3), Paquette MR(4), Driban JB(5), Vincent HK(6), Newman C(7), Messier SP(8), Ambrose KR(9), Shultz SP(10)(11). Exercise prescription for weight management in obese adults at risk for osteoarthritis: synthesis from a systematic review. BMC Musculoskelet Disord. 2019 Dec 20;20(1):610.

Doi: 10.1186/s12891-019-3004-3. PubMed PMID: 31861990; PubMed Central PMCID: PMC6925458: Free full text.

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ABSTRACT

BACKGROUND: The aim of this systematic review was to identify principles of exercise interventions associated with improved physical function, weight management or musculoskeletal pain relief among young and middle-aged adults with obesity and propose an evidence-based exercise prescription that could assist in secondary prevention of osteoarthritis.

METHODS: A structured electronic review was conducted using MEDLINE, PubMed, and SPORTDiscus. The search string included 1) "obes*" AND "exercise" AND "interven*" AND "musculoskeletal pain OR knee pain OR hip pain". Studies 1) were randomized controlled trials of humans, with a non-exercise control, 2) included participants aged 18-50 years, and 3) had outcomes that included physical function, musculoskeletal pain, and/or body composition. Studies were excluded if participants had peri-menopausal status, cancer, or obesity-related co-morbidities. A recommended exercise prescription was developed based on common principles used in the included exercise interventions with greatest change in function or pain.

RESULTS: Seven studies were included. Similarities in exercise intensity (40-80% VO2max), frequency (three times per week), duration (30-60 min), and exercise mode (treadmill, cross-trainer, stationary bike, aquatic exercise) were observed in exercise interventions that resulted in improved physical function and/or pain, compared to non-exercise control groups.

CONCLUSION: Common principles in exercise prescription for improvements in weight management, physical function and pain relief among otherwise healthy people with obesity. Exercise prescription including moderate intensity exercise for 30-60 min, three times per week can be considered an effective treatment for weight management and obesity-related musculoskeletal symptoms. Exercise should be recommended to at-risk individuals as part of secondary prevention of osteoarthritis.

READING 5 – BURDEN AND MANAGEMENT OF GOUT IN SINGAPORE

Chua CKT(1), Cheung PP(1)(2), Santosa A(1)(2), Lim AYN(1)(2), Teng GG(3)(4). Burden and management of gout in a multi-ethnic Asian cohort. Rheumatol Int. 2019 Nov 22.

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ABSTRACT

Gout has significant impact on the quality of life with over-utilisation of health resources. While lowering serum urate (SU) to≤360 μmol/L improves clinical outcomes, this is usually not achieved. We describe the burden of gout and determine predictors of achieving SU target in gout patients in Singapore.

This was a cross-sectional study of 282 gout patients from a Singapore hospital rheumatology service. Sociodemographic and lifestyle factors, co-existing medical conditions and medications, gout history and severity, SU levels and treatment were obtained. Patients with SU≤360 μmol/L were compared with those>360 μmol/L to determine factors associated with achieving SU target. Descriptive statistics and multivariate model were used.

Severe disease was reported in 50%, with emergency attendances and hospitalisations in 33% and 19% respectively, and unemployment in 32%. Only 22% were at SU target and 67% on urate-lowering therapy (ULT) at recruitment. Hypertension, dyslipidaemia, chronic kidney disease and diabetes were prevalent in 56.7%, 48.2%, 32.3% and 18.8%, respectively. Malays had more comorbidities compared to Chinese participants. In multivariate analysis, ULT prescription and≥2 comorbidities were associated with reaching SU target with odds ratios of 3.92 [95% confidence interval (CI) (1.75-8.71)] and 2.65 [95% CI (1.59-4.43)] respectively, independent of age, tophi, disease duration, body mass index, alcohol and diuretic use.

Patients with gout have high disease burden resulting in significant healthcare utilisation. SU control is sub-optimal hence the use of ULT remains key in achieving SU target. Patients with other comorbidities are more likely to reach target than those with only gout as a single diagnosis.

READING 6 – EVIDENCE FOR TREAT-TO-TARGET SERUM URATE IN GOUT

Bursill D(1), Dalbeth N(2). What Is the Evidence for Treat-to-Target Serum Urate in Gout? Curr Rheumatol Rep. 2018 Mar 8;20(3):11.

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ABSTRACT

PURPOSE OF REVIEW: Most current clinical guidelines for gout management advocate a treat-to-target serum urate approach, although notable differences exist. Serum urate is a rational target for gout treatment given the central role of urate in disease causality, its association with key outcomes and its practicality of use in clinical practice. This review analyses the evidence for this strategy in gout.

RECENT FINDINGS: Recent studies have confirmed the efficacy of urate-lowering therapy in achieving serum urate targets, both in trials using fixed doses and those applying a treat-to-target strategy. In a limited number of long-term studies (>12-month duration), interventions that incorporate a treat-to-target serum urate approach have been shown to promote regression of tophi, reduce the frequency of gout flares and improve MRI-detected synovitis.

A strong case can be made for a treat-to-target serum urate strategy in gout, supported by existing knowledge of disease pathophysiology, outcomes from urate-lowering therapy studies and emerging results of randomised strategy trials of sufficient duration.

READING 7 – CHRONIC GOUT BARRIERS TO EFFECTIVE MANAGEMENT

Rogenmoser S(1), Arnold MH(2). Chronic gout: Barriers to effective management. Aust J Gen Pract. 2018 Jun;47(6):351-356.

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ABSTRACT

BACKGROUND: Gout is one of the most common inflammatory arthropathies, and the pathogenesis is well understood. In Australia, most patients with chronic tophaceous gout (CTG) are treated by general practitioners (GPs). Urate-lowering therapy, if adhered to continuously, can suppress the disease, reduce the likelihood of flares and prevent long-term complications such as disfiguring tophi and joint damage. Many rheumatology societies recommend a treat-to-target (T2T) approach, lowering serum urate to 0.35 mmol/L or below with urate lowering therapy.

OBJECTIVE: The aim of this article is to discuss inconsistencies in treatment guidelines, identify patient and physician barriers to optimal gout care, explain why a T2T approach is appropriate and make a series of recommendations that are practical for GPs.

DISCUSSION: Despite an in-depth understanding of this controllable disease and the availability of simple, safe treatments, chronic gout remains poorly managed. The development of Australian gout guidelines that are easily implemented by GPs is vital and overdue.

READING 8 – MANAGING NON-ALCOHOLIC FATTY LIVER DISEASE

Libman H(1), Jiang ZG(1), Tapper EB(2), Reynolds EE(1). How Would You Manage This Patient With Nonalcoholic Fatty Liver Disease?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2019 Aug 6;171(3):199-207.

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ABSTRACT

Nonalcoholic fatty liver disease (NAFLD), a common diagnosis in the United States and other developed countries, has been increasing in prevalence.

The American Association for the Study of Liver Diseases recently published updated practice guidelines for diagnosing and managing NAFLD, including the following recommendations: Routine screening for NAFLD in high-risk groups is not advised because of uncertainties surrounding test and treatment options, along with a lack of knowledge about cost-effectiveness and long-term benefits.

Noninvasive studies, including biomarkers from laboratory tests and liver stiffness measured through elastography, are clinically useful tools for identifying advanced fibrosis in patients with NAFLD. Liver biopsy should be considered in patients with NAFLD who are at increased risk for nonalcoholic steatohepatitis (NASH) or advanced fibrosis.

Weight loss of at least 3% to 5% generally reduces NASH, but greater weight loss (7% to 10%) is needed to improve most histopathologic features, including fibrosis. Pharmacologic therapies (such as pioglitazone and vitamin E) should be considered only in patients with biopsy-proven NASH. Patients with NAFLD should not consume heavy amounts of alcohol, although insufficient data exist to provide advice about other levels of alcohol use.

Here, 2 clinicians with expertise in this area debate whether to screen for NAFLD in primary care, how to monitor patients with NAFLD, and what interventions should be used to manage this condition.

READING 9 – TACKLING HEART FAILURE WITH PRESERVED EJECTION FRACTION

Naing P(1), Forrester D(2), Kangaharan N(3), Muthumala A(4), Mon Myint S(5), Playford D(6). Heart failure with preserved ejection fraction: A growing global epidemic. Aust J Gen Pract. 2019 Jul;48(7):465-471.

doi: 10.31128/AJGP-03-19-4873. PubMed PMID: 31256507: Free full text..

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ABSTRACT

BACKGROUND: Heart failure with preserved ejection fraction (HFpEF) is an emerging global health problem of which there is limited awareness. HFpEF has a prognosis similar to that of heart failure with reduced ejection fraction (HFrEF) and accounts for approximately half of all patients with heart failure.

OBJECTIVE: The aim of this article is to review HFpEF and its consequences and management, including examples of patients with HFpEF.

DISCUSSION: Patients with HFpEF may present with dyspnoea, fluid retention, lethargy and dizziness, making it difficult to differentiate clinically from HFrEF. The risk factors include increasing age, obesity, hypertension, diabetes, chronic kidney disease and obstructive sleep apnoea. The diagnosis requires good clinical acumen combined with echocardiography and elevated plasma B-type natriuretic peptide concentration. Management of HFpEF, especially in later stages, is difficult as there is no evidence-based therapy to date. Prevention is the best strategy. Early recognition and diagnosis are also very important to tackle this global epidemic.

READING 10 – NITRATE USE RISK IN HEARTFAILURE WITH PRESERVED EJECTION FRACTION

Tsujimoto T(1), Kajio H(2). Use of Nitrates and Risk of Cardiovascular Events in Patients With Heart Failure With Preserved Ejection Fraction. Mayo Clin Proc. 2019 Jul;94(7):1210-1220. Free full text.

doi: 10.1016/j.mayocp.2018.11.032. PubMed PMID: 31272569: Free full text.

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ABSTRACT

OBJECTIVE: To assess the association of nitrate use with cardiovascular events in patients with heart failure with preserved ejection fraction (HFpEF).

PATIENTS AND METHODS: Patient data were collected from the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist trial, which had been conducted at 233 sites in 6 countries from August 10, 2006, through January 31, 2012. The primary outcome was the occurrence of a major adverse cardiovascular event (cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke) or heart failure hospitalization. The association between nitrate use and cardiovascular risk was evaluated using Cox proportional hazards analysis. In addition, we verified the results using propensity score-matched patients.

RESULTS: A total of 3417 patients with HFpEF were evaluated over a mean follow-up of 3.1 years, and 778 experienced a primary outcome event. The risk of primary outcome events was significantly higher in patients taking nitrates than in those not taking nitrates (hazard ratio [HR], 1.21; 95% CI, 1.01-1.46, P=.04). The risk of major adverse cardiovascular events was significantly higher in patients taking nitrates than in those not taking nitrates (HR, 1.32; 95% CI, 1.05-1.66, P=.01). Furthermore, the risk of hospitalization for heart failure was higher in patients taking nitrates (HR, 1.25; 95% CI, 0.99-1.60, P=.06), with propensity score-matched analyses revealing similar findings. In addition, a similar association was observed in various subgroups.

CONCLUSION: This study reported that nitrate use in patients with HFpEF was associated with a significantly increased risk of cardiovascular events.