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The 1-h post-load plasma glucose as a novel biomarker for diagnosing dysglycemia

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Abstract

Identifying the earliest moment for intervention to avert progression to prediabetes and diabetes in high-risk individuals is a substantial challenge. As β-cell function is already compromised in prediabetes, attention should therefore be focused on identifying high-risk individuals earlier in the so-called pre-prediabetes stage. Biomarkers to monitor progression and identify the time point at which β-cell dysfunction occurs are therefore critically needed. Large-scale population studies have consistently shown that the 1-h plasma glucose (1-h PG) ≥ 155 mg/dl (8.6 mmol/l) during the oral glucose tolerance test detected incident type 2 diabetes and associated complications earlier than fasting plasma glucose or 2-h plasma glucose levels. An elevated 1-h PG level appears to be a better alternative to HbA1c [5.7–6.4% (37–47 mmol/mol)] or traditional glucose criteria for identifying high-risk individuals at a stage when ß-cell function is substantially more intact than in prediabetes. Diagnosing high-risk individuals earlier proffers the opportunity for potentially reducing progression to diabetes, development of microvascular complications and mortality, thereby advancing benefit beyond that which has been demonstrated in global diabetes prevention programs.

Keywords

Dysglycemia; Prediabetes; Diabetes; Oral glucose tolerance test

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Introduction

The International Diabetes Federation (IDF) estimates that globally 425 million individuals, or 8.8% (1 in 11 adults) have diabetes (T2DM) with 629 million adults or 9.9% of the world's population expected to develop diabetes by 2045 [1]. In addition, 7.3% of the world's population or 352 million have impaired glucose tolerance (IGT) and are considered at high risk for developing diabetes with an expectation that this will increase to 532 million, or 8.3%, in 2045 [1]. Forty percent of adults face a lifetime risk of diabetes representing a substantial increase from 20% in the late 1980s [2]. Delaying the diagnosis can result in at least one complication by the time an individual has been diagnosed. Herman et al. [3] demonstrated a 29% relative risk reduction (RRR) in cardiovascular disease (CVD) outcomes and a 17% RRR in all-cause mortality after 5 years among screened individuals undergoing routine care compared with a 3-year delay in diagnosis and treatment illustrating the beneficial effects accrued from early diagnosis and identification of high-risk individuals. Furthermore, screening for glucose intolerance in high-risk populations and implementing interventions have been shown to be cost-effective [4].

Finally, from 2007 to 2012, approximately 7.9 million individuals in the USA with diabetes were unaware of their diagnosis although 85% had access to a care provider [5]. Therefore, identifying high-risk individuals at an earlier time point is of paramount importance.

Caveats in diagnosing dysglycemic states

The dysglycemic or prediabetic conditions referred to as categories of increased risk for future development of T2DM include impaired fasting glucose (IFG) and IGT.

Defining prediabetes is controversial as different glucose and HbA1c criteria have been posited by the American Diabetes Association (ADA), International Expert Committee (IEC) and World Health Organization (WHO) with differing thresholds, sensitivities, specificities, morbidity and mortality hazard ratios [6] (Table 1). The various definitions therefore identify different but overlapping populations. These inadequacies led to a recent commentary underscoring the need for a more precise, evidence-based definition of intermediate hyperglycemia [6].

Current diagnostic thresholds for T2DM [FPG > 126 mg/dl (7.0 mmol/l) and 2-h plasma glucose > 200 mg/dl (11.1 mmol/l)] are largely based on an association of cross-sectional glycemic levels with diabetic retinopathy [7]. The International Expert Committee (IEC) [8], the ADA [9] and WHO [10] proposed a HbA1c threshold value of 6.5% (47.5 mmol/mol) for diagnosing diabetes also based on studies demonstrating an association between HbA1c and diabetic retinopathy. Discordance between HbA1c and glycemic measures has been observed as they represent different physiologic processes [11]. For example, the US National Health and Nutrition Examination Survey (NHANES-3) from 2005 to 2006 showed that the HbA1c ≥ 6.5% (47.5 mmol/mol) identified one-third fewer cases of undiagnosed diabetes than a FPG ≥ 126 mg/dl (7.0 mmol/l) [12].

The risk of future outcomes across different prediabetes definitions based on fasting glucose concentration, HbA1c, and 2-h glucose concentration was assessed in the community-based

Atherosclerosis Risk in Communities (ARIC) study. The WHO fasting glucose concentration threshold [110–125 mg/dl (6.1–6.9 mmol/l)] and HbA1c-based definitions of prediabetes resulted in lower prevalence estimates than ADA fasting glucose concentration [100–125 mg/dl (5.6–6.9 mmol/l)] and ADA and WHO 2-h glucose concentration cutoffs [140–199 mg/dl (7.8–11.0 mmol/l)]. However, these were more specific in identifying people at risk for long-term outcomes. ADA fasting glucose and ADA and WHO 2-h glucose definitions of prediabetes were found to be more sensitive for long-term outcomes. Furthermore, HbA1c-based definitions of prediabetes showed stronger associations with long-term outcomes for many major clinical complications. Differences between definitions using both ADA and WHO fasting glucose concentrations for long-term risk associations were not observed when compared with ADA and WHO 2-h glucose concentration cutoffs [13]. The ARIC study also demonstrated that the glycated hemoglobin, in addition to being associated with risk of diabetes, was more strongly associated with risks of cardiovascular disease and death from any cause compared with fasting glucose [13].

Gaps in identifying individuals at high risk for progression to prediabetes and diabetes

Identifying the earliest moment in which to intervene to avert progression to prediabetes and diabetes in high-risk individuals is a substantial challenge. As β-cell function is already substantially impaired in prediabetes based on current definitions [14-17], attention should therefore be focused on identifying individuals with prediabetes even earlier [18]. Biomarkers to monitor progression and identify the time point at which β-cell dysfunction occurs are therefore critically needed [19, 20]. Fasting and post-load glucose levels increased as early as 13 years before diabetes developed in the Whitehall II Study although remaining within the normal range until 2–6 years before diagnosis at which time these levels increased dramatically [21]. Insulin sensitivity was reduced for 13 years and fell steeply 5 years before diagnosis of diabetes. Insulin secretion remained constant until substantial compensation occurred 3–4 years prior to a steep decline prior to diagnosis.

Hence, β-cell function declines in the prediabetic state many years before diabetes develops. As fasting and postprandial glucose concentrations follow a continuum, it is plausible that lifestyle intervention initiated before current absolute thresholds for prediabetes are achieved and when β-cell function is likely more intact it could be even more effective in preventing progression to diabetes. In fact, lack of progression during the Diabetes Prevention Program (DPP) was related to frequency of regression to normoglycemia [22]. Furthermore, lifestyle intervention was significantly more successful in those with lower baseline glucose concentrations [23]. Use of absolute thresholds for diagnosing subtle dysglycemic states may therefore have the unintended consequence of limiting detection and intervention which may be make reversibility less likely [23].

Current absolute definitions of prediabetes remain inadequate as these identify individuals rather late in the dysglycemic continuum, thereby missing an opportunity for earlier intervention when β-cell functionality is more intact [19, 23]. Clearly, harmonization would be contingent on identifying a biomarker characterized by optimal specificity and sensitivity,

the ability to diagnose high-risk individuals early in the trajectory to diabetes before β-cell functionality is substantially impaired, as well as the capability of predicting progression to T2DM, complications and mortality. This review will focus on the 1-h post-load plasma glucose during the OGTT as a biomarker fulfilling these characteristics.

The 1-h post-load plasma glucose during the OGTT

Evidence from large-scale population studies has consistently shown that the 1-h plasma glucose (1-h PG) ≥ 155 mg/dl (8.6 mmol/l) during the OGTT may detect incident T2DM and associated complications better than FPG or 2-h PG levels. Published studies investigating the 1-h PG studies are summarized in Table 2. Abdul Ghani et al. [24] demonstrated the predictive power of the 1-h PG level versus FPG and 2-h PG values with incident diabetes over 8 years in a high-risk Mexican-American cohort. They also recommended the 1-h PG threshold of ≥ 155 mg/dl (8.6 mmol/l) and ATP III criteria for the metabolic syndrome in order to stratify high-risk individuals [24]. The Botnia Study and the Malmö Preventive Project provided evidence that fasting glucose, 2-h PG and glucose tolerance status were less efficient predictors than 1-h PG of incident T2DM. The authors concluded that the 1-h PG was a more efficient screening tool to select high-risk individuals for developing T2DM risk [25].

A series of sub-analyses from the CATAnzaro MEtabolic RIsk factors (CATAMERI) study provided further novel insights into the 1-h PG on diabetes and cardiovascular risk factors. The study showed that individuals with NGT and the 1-h PG ≥ 155 mg/dl (8.6 mmol/l) were predisposed to an increased risk for developing diabetes over a 5-year period [26], chronic kidney disease [27], increased risk of non-alcoholic fatty liver disease diagnosed by ultrasonography [28] and increased vascular stiffness [29] than those with IFG or NGT and 1-h PG < 155 mg/dl (8.6 mmol/l). Mechanistically, sub-analyses also showed an association between NGT individuals and 1-h PG ≥ 155 mg/dl (8.6 mmol/l) with elevated liver enzymes [30], adverse atherogenic profile [31, 32], lower vitamin D concentrations [33], decreased insulin clearance [34], insulin sensitivity and reduced β-cell function [35] and unfavorable inflammatory profile [36] (Table 3).

The accuracy of HbA1c and the 1-h PG versus the OGTT was compared in a real-life clinical setting and found that the level of agreement was twofold greater for the 1-h PG ≥ 155 mg/dl [8.6 mmol/l (95% CI): 0.40[0.28–0.53)] than HbA1c categories defined by the ADA [HbA1c: 5.7–6.4%(39–46 mmol/mol); 0.1(0.03–0.16)] and the IEC [HbA1c: 6.0–6.4% (42–46 mmol/mol); 0.17(0.04–0.30)] [37]. Importantly, the 1-h PG showed a stronger association with 2-h PG, insulin sensitivity index and β-cell function than HbA1c ($P < 0.05$). The Israel Study of Glucose Intolerance, Obesity and Hypertension (The Israel GOH Study) observational study cohort followed over 24 years demonstrated that individuals with a 1-h PG ≥ 155 mg/dl (8.6 mmol/l) but with 2-h PG < 140 mg/dl (7.8 mmol/l) had a significantly elevated risk of both diabetes (OR: 4.35, 95%CI 2.50–7.73) and prediabetes (OR = 1.87, 95%CI 1.09–3.26) after adjusting for sex, age, smoking, body mass index, blood pressure, fasting blood glucose and insulin [38]. In the same cohort, the 1-h PG > 155 mg/dl (8.6 mmol/l) was found to predict mortality even when the 2-h PG was < 140 mg/dl (7.8 mmol/l) after adjusting for sex, age, smoking, body mass index, systolic and diastolic blood pressure.

Risk of both progression and mortality were even greater in those with *both* an elevated 1-h PG *and* IGT [39]. The Malmö Preventive Project similarly found increased risk of progression to diabetes, microvascular disease and mortality during a 39-year follow-up in those with a 1-h ≥ 155 mg/dl (8.6 mmol/l) [40]. Therefore, these observations would suggest that the 1-h PG > 155 mg/dl (8.6 mmol/l) may be important for the earlier detection of high-risk individuals to avert T2DM and complications. However, precise estimates regarding how much earlier lifestyle intervention could be initiated with the new 1-h PG definition are difficult to assess in the absence of a prospective trial specifically addressing this question.

Conclusions

As dysglycemic conditions are continuous and cannot be defined by absolute thresholds [23], current diagnostic parameters largely preclude early identification of individuals at high risk for progressing to T2DM. Therefore, prediabetes is diagnosed when β-cell dysfunction is proximal to the development of T2DM. A shift to diagnosing high-risk individuals even earlier offers the potential opportunity for further reducing progression to diabetes, development of microvascular complications and mortality, thereby advancing benefit beyond what has been demonstrated in global diabetes prevention programs. The considerable consistent and significant epidemiologic evidence from different populations substantiates the conclusion that an elevated 1-h PG level appears to be a better alternative for identifying high-risk individuals at a stage when ß-cell function is substantially more intact than in prediabetes.

The 1-h PG level has been associated with adverse biologic properties and has been shown to be a marker for subclinical target organ damage (Table 3). Furthermore, as discussed earlier, the 1-h PG possesses desirable characteristics for an optimal biomarker. In addition, shortening the OGTT to 1 h should facilitate its use in clinical practice to avoid underdiagnosing high-risk individuals. Therefore, the aggregate of findings support the proposal that a 1-h PG level ≥ 155 mg/dl (8.6 mmol/l) should be considered for adoption into clinical practice as to earlier detect progression to worsening dysglycemia and mortality [38-40].

Finally, since any single biomarker, including the 1-h PG ≥ 155 mg/dl (8.6 mmol/l), may have limitations, combining biomarkers may provide better sensitivity and specificity for more precisely detecting those at high risk for developing dysglycemia. Additional comparison studies of biomarkers will therefore be required to ascertain their clinical utility [41].

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Table 1

Different classifications of prediabetes. Adapted from Ref. [6]

	Impaired fasting glucose	Impaired glucose tolerance	Sub-diabetic HbA1c
ADA (2010)	100–125 mg/dl (5.6–6.9 mmol/L)	140–199 mg/dl (7.8–11.0 mmol/L)	5.7–6.4% (39–46 mmol/mol)
WHO (1999)	110–125 mg/dl (6.1–6.9 mmol/L)	140–199 mg/dl (7.8–11.0 mmol/L)	–
IEC (2009)	–	–	6.0–6.4% (42–46 mmol/mol)

ADA American Diabetes Association, *WHO* World Health Organization, *IEC* International Expert Committee

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Table 2

Summary of 1-h plasma glucose publications

Author (Year)	Country	Cohort characteristics						Study objectives	Findings
		Sample size (*n*)	Age (Y)	Male (*n*, %)	Prevalence 1-h PG > 155 mg/dl (*n*, %)	BMI (kg/m^2)	Study design		
Vaccaro (1992) [42]	USA	873	51.1 ± 7.7	873	NA	27.1 ± 3.5	Chicago People Gas Company study; mean follow-up: 19 years	Examining the relationship 1 h post-load versus 2 h post-load PG measurements to mortality	Outcome: coronary artery disease 1-h $PG_{>195mg/dl}$ versus 1-h $PG_{<100mg/dl}$ HR [95%CI]: 1.76[0.97–3.20] Outcome: cardiovascular disease 1-h $PG_{>195mg/dl}$ versus 1-h $PG_{<100mg/dl}$ HR [95%CI]: 1.96[1.11–3.45] Outcome: all causes mortality 1-h $PG_{>195mg/dl}$ versus 1-h $PG_{<100mg/dl}$ HR [95%CI]: 1.56[1.06–2.30]
Abdul Ghani (2008) [24]	USA	1301	42.0 ± 11.0	559 (43)	217 (16.7)	27.1 ± 5.1	San Antonio Heart Study. Mean follow-up duration: 8 years	Assessing the efficacy of 1-h plasma glucose concentration and the metabolic syndrome in predicting future risk of T2DM	Outcome: Diabetes (a) without metabolic syndrome $NGT_{1\text{-h PG} > 155mg/dl}$—metabolic syndrome vs. $NGT_{1\text{-h PG}<155 mg/dl}$ HR [95%CI]: 3.4[1.8–6.4] (b) $NGT_{1\text{-h PG} > 155 mg/dl}$ + metabolic syndrome vs. $NGT_{1\text{-h PG} < 155 mg/dl}$ HR [95%CI]: 15.2[7.8–29.3]
Cubbedu et al. (2010) [43]	Venezuela	327	39.4 v. 47 ($p < 0.05$)	Not specified	25 (7.6%)	28.5 v. 29.2 ($p < 0.05$)	Latino–Hispanics	1-h OGTT to predict increased risk of T2DM and surrogate markers of insulin	$NGT_{1\text{-h PG} < 155 mg/dl}$ vs. $NGT_{1\text{-h PG} > 155 mg/dl}$ HOMA-IR: 2.87 v. 2.66 (not significantly different) Matsuda index: 3.42 v. 2.51 ($p < 0.05$) Disposition index: 0.82 v. 0.49 ($p < 0.01$)
Manco et al. (2010) [44]	Europe	1100	43.0 v. 45.39 ($p < 0.001$)	? 56.1% women of total sample would include IGT group	222 (20.2%)	24.9 v. 26.25	RISC study	To correlate 1-h PG levels with beta cell function	$NGT_{1\text{-h PG}<155 mg/dl}$ vs. $NGT_{1\text{-h PG}> 155 mg/dl}$ Beta cell glucose sensitivity: 153.1 v. 86.88 ($p < 0.001$) B-cell rate sensitivity: 1150.2 v. 781.8 ($p < 0.001$) Potentiation factor: 2.2 v. 1.9 ($p < 0.001$)
Marini et al. 2017 [45]	Europe	256	35 v. 40 ($p < 0.0001$)	100 (39.0%)	72 (28.1%)	28.8 v. 30.1 ($p = 0.72$)	nondiabetic offspring participating in the EUGENE2 (European Network on Functional Genomics of Type 2 Diabetes) project who had one parent with type 2 diabetes	To study the association between 1-h PG levels and blood viscosity	$NGT_{1\text{-h PG}<155 mg/dl}$ vs. $NGT_{1\text{-h PG}>155 mg/dl}$ Matsuda index: 5.89 v. 3.7 ($p < 0.0001$) Insulin-stimulated glucose disposal: 11.3 v. 8.9 ($p = 0.01$) Disposition index: 4708 v. 2945 ($p < 0.0001$)

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Author (Year)	Country	Cohort characteristics						Study objectives	Findings
		Sample size (*n*)	Age (Y)	Male (*n*, %)	Prevalence 1-h PG > 155 mg/ dl (*n*, %)	BMI (kg/m^2)	Study design		
							and one parent without a history of type 2 diabetes		
Succurro et al. (2010) [27]	Italy	1003	49.0 ± 12.0	475 (47.4)	445 (44.3)	30.3 ± 5.9	CATAMERI study cohort. Cross-sectional design	Assessing 1-h PG levels as a predictor of CKD	Outcome: Chronic kidney disease $NGT_{1\text{-h PG} > 155\ mg/dl}$ vs. $NGT_{1\text{-h PG} < 155\ mg/dl}$ OR [95%CI]: 2.61 [1.01–6.77]
Strandberg (2011) [46]	Finland	2756	42	2756		25.7	Helsinki Businessmen Study	Assessing development of diabetes and mortality using the 1-h plasma glucose test in conjunction with BMI	Outcome: Diabetes. $NGT_{1\text{-h PG}>161\ mg/dl}$ and BMI ≥ 25 kg/m^2 vs. $NGT_{1\text{-h PG}<161\ mg/dl}$ and BMI < 25 HR [95%CI]: 2.27 [1.67-3.08] $NGT_{1\text{-h PG}>161\ mg/dl}$ and BMI < 30.0 kg/m^2 vs. $NGT_{1\text{-h PG}<161\ mg/dl}$ and BMI < 25. HR [95%CI]: 4.71 [3.36–6.60] $NGT_{1\text{-h PG} > 161\ mg/dl}$ and BMI ≥ 30.0 kg/m^2 vs. $NGT_{1\text{-h PG}<161\ mg/dl}$ and BMI < 25. HR [95%CI]: 10.13 [6.46-15.89] Outcome: mortality $NGT_{1\text{-h PG} > 161\ mg/dl}$ and BMI ≥ 25 kg/m^2 vs. $NGT_{1\text{-h PG}<161\ mg/dl}$ and BMI < 25 HR [95%CI]: 1.14[1.00–1.29] $NGT_{1\text{-h PG} > 161\ mg/dl}$ and BMI < 30.0 kg/m^2 vs. $NGT_{1\text{-h PG} < 161\ mg/dl}$ and BMI < 25. HR [95%CI]: 1.19[1.00-1.41] $NGT_{1\text{-h PG}>161\ mg/dl}$ and BMI ≥ 30.0 kg/m^2 vs. $NGT_{1\text{-h PG} < 161\ mg/dl}$ and BMI < 25. HR [95%CI]: 1.51 [1.13–2.02]
Fiorentino (2015) [26]	Italy	234	41.8 ± 10.8	100 (42.9)	60 (25.6)	28.7 ± 5.8	CATAMERI and EUGENE study cohort. Mean follow-up: 5.2 years	Evaluating 1-h PG levels predicts T2DM in NGT subjects compared to IFG.	Outcome: diabetes $NGT_{1\text{-h PG} > 155\ mg/dl}$ vs $NGT_{1\text{-h PG} < 155\ mg/dl}$ HR: 4.02 [1.06–15.26] Outcome: insulin-stimulated glucose disposal: 10.5 v. 8.4 ($p < .000$ includes isolated IFG and IGT) Disposition index: 265 v. 142 ($p < .000$ includes isolated IFG and IGT)
Priya (2013) [47]	India	1179	45.4 ± 10.6	734 (62.2)	502 (42.6)	26.3 ± 6.4	Data from primary care; mean follow-up duration: 4.0 years	Using the 1-h OGTT to predict progression to prediabetes and T2DM among those with NGT	Outcome: Prediabetes $NGT_{1\text{-h PG} > 155\ mg/dl}$ vs. $NGT_{1\text{-h PG} < 155\ mg/dl}$ proportion (n, %): 181 (28.9) vs. 211 (52.2) Outcome: diabetes $NGT_{1\text{-h PG} > 155\ mg/dl}$ vs. $NGT_{1\text{-h PG} < 155\ mg/dl}$ proportion (n, %): 98 (19.5) vs. 50 (8.0)

Author (Year)	Country	Cohort characteristics						Study objectives	Findings
		Sample size (*n*)	Age (Y)	Male (*n*, %)	Prevalence 1-h PG > 155 mg/ dl (*n*, %)	BMI (kg/m^2)	Study design		
Priya et al. (2016) [48]	India	166	20 v. 22 v 23 (p = 0.012)	46.1 v. 66.7 v. 46.7% (p = 0.094)	30 (18.1%)	24.1 v. 25.7 v. 25.2 (p = 0.817)	Data from specialized diabetes center in Chennai	Assessing B-cell function and insulin sensitivity indices among NT stratified by 1-h plasma glucose	NGT 1 h < 143 mg/dL v. 143 to < 155 mg/dL v ≥ 155 mg/dL HOMA-IR: 2.8 v. 3.4 v. 1.8 (p = 0.103) Insulinogenic index: 367 v. 257 v. 246 (p = 0.019) Matsuda index: 11.2 v. 7.4 v. 5.5 (p < 0.001) Insulin sensitivity index: 0.015 v. 0.012 v. 0.011 (p = 0.028)
Kim (2013) [49]	USA	233	11.1 ± 1.7	100 (42.9)	82 (35.2)	28.7 ± 5.5	Obese Latino youth with a family history of type 2 diabetes. Mean follow-up: 4.7 years	Examining the utility of elevated 1-h glucose levels to predict deterioration in B-cell function and the development of prediabetes	Outcome: prediabetes $NGT_{1\text{-h PG} > 155\ mg/dl}$ vs. $NGT_{1\text{-h PG} < 155\ mg/dl}$ OR [95%CI]: 2.4 [1.4–4.2] During the follow-up 1-h PG ≥ 155 mg/dL group exhibited a significantly greater decline in β-cell function compared with youth with a 1-h glucose < 155 mg/dL (β = −327.8 ± 126.2, p = 0.01)
Oh et al. (2015) [50]	South Korea	192	52.8 v. 53.7	46 (24.0%)	43 (22.4%)	23.8 v. 24.5	Cross-sectional	To study B-cell function in subjects with 1 h high and 1 h low	$NGT_{1\text{-h PG} < 155\ mg/dl}$ vs. $NGT_{1\text{-h PG} > 155\ mg/dl}$ HOMA-IR: 1.2 v. 1.4 (p = 0.148) Matsuda index: 9.3 v. 8.3 Oral disposition index: 2.5 v. 1.8 (p < 0.001) ISS-2: 301.2 v. 213 (p < 0.001) Insulinogenic index at 60 min was not significantly different between the groups
Bergman et al. (2016) [38, 39]	Israel	739	48.1 ± 6.7	376 (50.9)	188 (25.4)	25.5 ± 3.6	The Israel Study of glucose intolerance, obesity and hypertension. Mean follow-up duration: 24 years	Evaluating the association of an elevated 1-h PG with cumulative incidence of diabetes, prediabetes and mortality	Outcome: prediabetes 1-h $PG_{> 155mg/dl}$ and 2-h $PG_{< 140mg/dl}$ vs. 1-h $PG_{<155\ mg/dl}$ and 2-h $PG_{<140mg/dl}$ OR [95%CI]: 1.87 [1.09–3.26] Outcome: diabetes 1-h $PG_{>155\ mg/dl}$ and 2-h $PG_{<140mg/dl}$ vs. 1-h $PG_{<155\ mg/dl}$ and 2-h $PG_{<140mg/dl}$ OR [95%CI]: 4.35 [2.50–7.73] Outcome: mortality 1-h $PG_{> 155\ mg/dl}$ and 2-h $PG_{< 140mg/dl}$ vs. $PG_{<155\ mg/dl}$ and 2-h $PG_{<140mg/dl}$ OR [95%CI]: 1.28 [1.09–1.50]
Oh et al. (2017) [51]	Korea	5703	51.3 ± 8.7	3062 (53.4)	2435 (42.7)*	24.1 ± 3.1	Korean Genome and Epidemiology Study. Mean follow-up duration: 12 years	Assessing 1-h OGTT levels as a predictor of future T2DM compared to IGT	Outcome: diabetes $NGT_{1\text{-h PG}>145\ mg/dl}$ vs. $NGT_{1\text{-h PG}<145\ mg/dl}$ HR [95%CI]: 2.84[2.34–3.45]
Paddock et al. (2017) [52]	USA	1946	25.4	817 (42.0)	NA	30.0 ± 6.0	Southwestern Native American (SWNA) community in Arizona; Mean	Assessing 1-h PG as a predictor of T2DM along with insulin secretion	Outcome: Diabetes $NGT_{1\text{-h PG} > 168\ mg/dl}$ vs. $NGT_{1\text{-h PG} < 168\ mg/dl}$ HR [95%CI]: 1.71 [1.60–1.82]

Author (Year)	Country	Cohort characteristics						Study objectives	Findings
		Sample size (*n*)	Age (Y)	Male (*n*, %)	Prevalence 1-h PG > 155 mg/ dl (*n*, %)	BMI (kg/m^2)	Study design		
							follow-up duration: 12.8 years		
Pareek et al. (2018) [40]	Sweden	4703	48.0 (48.0–49.0)	4703 (100)	1564 (33.3)	24.8 ± 3.1	Population-based cohort study from Malmo, Sweden. Mean follow-up duration: 39 years	Evaluating 1-h PG as a predictor of T2DM, cardiovascular risk and mortality compared to 2-h level.	Outcome: diabetes $NGT_{1\text{-h PG > 155 mg/dl}}$ vs. $NGT_{1\text{-h PG > 155 mg/dl}}$ HR [95%CI]: 2.93 [2.48–3.46] Outcome: all-cause mortality $NGT_{1\text{-h PG > 155 mg/dl}}$ vs. $NGT_{1\text{-h PG < 155 mg/dl}}$ HR [95%CI]: 1.29 [1.19–1.39] Outcome: incident myocardial infarction and fatal ischemic heart disease $NGT_{1\text{-h PG > 155 mg/dl}}$ vs. $NGT_{1\text{-h PG < 155 mg/dl}}$ HR [95%CI]: 1.24 [1.10–1.39] Outcome: diabetic retinopathy $NGT_{1\text{-h PG > 155 mg/dl}}$ vs. $NGT_{1\text{-h PG < 155 mg/dl}}$ HR [95%CI]: 5.23 [3.24–8.43] Outcome: diabetic peripheral vascular complications $NGT_{1\text{-h PG > 155 mg/dl}}$ vs. $NGT_{1\text{-h PG < 155 mg/dl}}$ HR [95%CI]: 2.90 [1.69–4.99]

Table 3

Associations of the elevated 1-h glucose ≥ 155 mg/dL (8.6 mmol/L) with biologic markers and subclinical target organ damage

Impaired β-cell function
Insulin resistance
Adiposity
High lipid ratios
Increased WBC
Increased fibrinogen
Subclinical target organ damage
Subclinical atherosclerosis
Subclinical inflammation
Arterial stiffness
Carotid intima-media thickness
Left ventricular hypertrophy
Decline in kidney function
Fatty liver