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## Improved Detection of Prediabetes in African Immigrants

The International Diabetes Federation (IDF) predicts the world-wide prevalence of diabetes to increase by 109% by 2035. Various studies have established that lifestyle modifications in patients with well established diabetes do not impact all-cause mortality, cardiovascular events, or microvascular complications. On the other hand, lifestyle modifications during prediabetes can delay or prevent transition to diabetes. Therefore, effective screening programs for identification of pre-diabetic patients during routine annual examination may be important.

The diagnosis of diabetes, as defined by American Diabetes Association (ADA), requires presence of at least two of the three criteria, namely

1. Fasting plasma glucose (FPG)  $\geq 126$  mg/dL ( $\geq 7$  mmol/L)
2. 2-hour glucose  $\geq 200$  mg/dL ( $\geq 11.1$  mmol/L)
3. A1c  $> 6.5\%$

A recent study (*Diabetes Care* 2016;39:271-277) evaluated approximately 217 immigrants of African origin in the Bethesda, MD area using a prediabetes definition of FPG  $\geq 100$  mg/dL ( $\geq 5.6$  mmol/L) and  $\leq 125$  mg/dL ( $\leq 7$  mmol/L) and/or 2-hour glucose  $\geq 140$  mg/dL ( $\geq 7.8$  mmol/L) and  $\leq 199$  mg/dL ( $\leq 11.1$  mmol/L), or 2-hour glucose of  $> 199$  mg/dL ( $\geq 11.1$  mmol/L) in the absence of a second criteria. In addition to A1c, serum fructosamine and glycated albumin (GA) were determined in these individuals to account for presence of hemoglobin variants including sickle cell disease, or compound heterozygotes including hemoglobin SC. The upper tertile of the reference range for fructosamine and GA were used as the cut-off to define prediabetes ( $> 230$   $\mu$ mol/L and  $> 13.35\%$ , respectively). The overall prevalence of prediabetes in study participants using the oral glucose tolerance (OGTT) criteria was found to be 34%. These individuals were older with higher BMI, waist circumference (WC), and more visceral adipose tissue (VAT) (measured by abdominal computed

tomography scans at level of L2-3). Other parameters including degree of insulin resistance measured by Matsuda index and beta-cell function measured by the oral disposition index were worse in prediabetic individuals.

Further characterization of the prediabetic individuals revealed three patterns -

1. detected by higher A1c levels only
2. detected by higher A1c and fructosamine/GA levels

3. detected by higher fructosamine/GA levels only

Individuals in group 1 and 3 had no difference in measurements of OGTT, 2-hour glucose levels, Matsuda index, insulinogenic index, or the oral disposition index. However, physical parameters including age, BMI, WC, and VAT were significantly different in both the groups. The individuals identified with glycated plasma proteins only were younger, and had lower BMI, smaller WC, and less VAT compared to individuals identified by A1c. Frequency of hemoglobin variants and albumin levels were similar in these two groups.

Findings of this study are consistent with reports from East Asia (Ikezaki H, *et. al.* *Metabolism* 2015;64:698-705 and Nishimura R, *et. al.* *Diabetes Res Clin Pract* 2006;71:334-338) and underscore the importance of an inverse relation between GA and BMI. Extrapolating from these observations, it is theorized that measurement of GA may enhance detection of prediabetes in certain ethnic groups. The final conclusion of these studies is superior performance of A1c when combined with GA instead of FPG in detection of prediabetes.

## ABO Compatibility and Platelet Transfusions

Because there is a small amount of residual plasma in RBC units, only major ABO compatibility is considered while issuing packed RBC units. But platelet products contain a significant amount of plasma, therefore both major and minor ABO compatibility must be considered in issuing units.

Major mismatches, in which the recipient has natural antibodies against the transfused platelet ABO type, are associated with reduced post transfusion platelet increments. However, this has not been shown to be associated with adverse clinical outcomes in patients (Trizulzi, DJ, Blood 2012;119(23),5553-5562). Minor mismatches, in which donor plasma present in the platelet product has natural antibodies against the recipient's RBC ABO type, have been implicated in non-fatal and rare fatal hemolytic transfusion reactions. The most common implicated donors in such cases are group-O with high titer anti-A/anti-B antibodies. These reactions are rare enough to have no significant impact on clinical practice (Lin Y, Transfusion 2002;42:166-72).

ABO identical platelet transfusions are ideal, but not always possible due to platelet inventory issues (minimizing product wastage due to outdating), the short shelf life of platelets (5 days) and supply restrictions.

To provide optimal patient care, Saint Luke's Health System issues ABO identical apheresis platelets whenever possible. If ABO identical platelets are not available, ABO compatible platelets may be considered, as outlined in the table below. If the patient requires more than one ABO non-identical platelet in a 24 hour period, the pathologist can be consulted for transfusion recommendations.

Patient Type	1 <sup>st</sup> choice	2 <sup>nd</sup> choice	3 <sup>rd</sup> choice
O	O	AB	A
A	A	AB	B
B	B	AB	A
AB	AB	A	B

In emergent situations, physicians should consider the risks and benefits of delaying the transfusion while waiting for ABO identical platelets versus probable smaller increment increase or hemolytic reaction from ABO non-identical platelets.

## Effect of Renal Function on Direct Oral Anticoagulant Dosing

Direct oral anticoagulants (DOAC) are approved for multiple thromboembolic disorders and afford multiple advantages over existing agents including no increased risk of clinically relevant bleeding or requirement for regular laboratory monitoring. Similar to other kidney-excreted drugs, DOACs may require dose-adjustment based on glomerular filtration rate (GFR).

The prescribing information provided by the US Food and Drug Administration (FDA) and the dosing recommendations in The North American Thrombosis Forum AF Action Initiative Consensus Document, are based on creatinine clearance (CrCl) expressed in mL/min. Importantly, it is recommended that patients with CrCl <30mL/min should not take DOACs because of potential accumulation. Detailed discussions of renal impairment, dose reductions, and contraindications in subsequent chapters of the Document, use CrCl and GFR interchangeably. In routine clinical practice, CrCl and eGFR are not synonymous and are estimated using different serum creatinine-based equations. CrCl expressed in mL/min is estimated using the Cockcroft-Gault equation which also incorporates patient weight. By contrast, GFR or estimated GFR (eGFR), expressed in mL/min/1.73 m<sup>2</sup>, is calculated using 4-variable Modification of Diet in Renal Disease or Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations and incorporates patient ethnicity.

Since most clinical laboratories report eGFR, as recommended by the Clinical Practice Guidelines for the Evaluation and Management of Chronic Kidney Disease, the use of eGFR interchangeably with CrCl may result in inappropriate DOAC dose adjustment or reduction in unqualified patients. These observations have been reported recently in numerous publications (Fernandez-Prado *et. al.* Am J Med. 2016;129:1259-1263).

Further, as noted by the authors, patient outcomes in routine clinical practice may differ from randomized clinical trials, because use of eGFR criteria identifies different patient populations. A careful monitoring of safety and efficacy of such practice is required either through routine clinical registries or ideally, through new clinical trials to prevent risk of DOAC dose adjustment in unqualified patients.