KDIGO Controversies Conference

Diabetic Kidney Disease

16-18 March, 2012
New Delhi, India

CONFERENCE OVERVIEW

The incidence and prevalence of diabetes mellitus continue to grow dramatically throughout the world, due primarily to the increase in type 2 diabetes (T2DM), which in turn is largely related to the increase in obesity (1). This increase in T2DM disproportionately affects less developed countries, which also have fewer resources to deal with such patients (1). Although improvements in diabetes and hypertension management have reduced the proportion of diabetic individuals who develop chronic kidney disease (CKD) and who progress to ESRD (2), the sheer increase in the numbers developing diabetes will perforce have a major impact on dialysis and transplant needs. The competing outcome of cardiovascular disease (CVD) mortality is also of tremendous importance.

Because of this dramatic increase in the number of individuals developing diabetes, it is important to develop cost-effective strategies at every step: (1) prevention of obesity; (2) screening for and prevention of diabetes in an at-risk population; (3) glycemic control once diabetes develops; (4) blood pressure control once hypertension develops; (5) screening for diabetic CKD; (6) use of renin angiotensin aldosterone system (RAAS) inhibition/blockade in those with diabetic CKD; and (7) control of other cardiovascular risk factors such as management of LDL cholesterol.

The relationship of CKD to CVD remains complex. Increased urinary albumin excretion rates and decreased GFR are both associated with an increase in all-cause and CVD mortality independent of each other and of other CVD risk factors in general and high-risk populations (3-5). The relationship between the presence of microalbuminuria and CVD mortality in diabetic individuals has been known for over 25 years (6) and the interrelationship between AER, GFR and CVD mortality has been well-studied in diabetic individuals (7,8). However, treatments that affect progression of CKD may not always have the same effect on the development/progression of CVD. Similarly, there may be differences in how interventions affect urinary AER vs. GFR. In patients with diabetes, there appear to be differences in the rate of progression of the fall in GFR that are related to the presence or absence of increased AER (8,9).

Studies in both T1DM and T2DM have shown that glycemic control can decrease the initial development of micro- and macroalbuminuria (10-13), but data documenting an effect on GFR are sparse (14-17). Recent data suggest that perhaps there should be different hemoglobin A1c (HbA1c) targets for CKD and CVD, as HbA1c levels below 7% continue to show benefit in preventing the development of microalbuminuria (18-20) but show no benefit (18-20) and perhaps harm (21) with respect to CVD. Although there may be only a minimal effect of lower HbA1c levels on CKD as it progresses towards Stage 5, other complications of DM, such as retinopathy and neuropathy may benefit from such control.

Similarly, the blood pressure targets for CKD and CVD may be different. While it is recognized that blood pressure control is very important in slowing the rate of fall of GFR (22), at this point, the optimal blood pressure to benefit all outcomes is controversial. Similar to the effects of glycemic control, systolic BP (SBP) lower than 120 mmHg may be of further benefit for CKD progression (23), but may be associated with worsened CVD outcomes (23-25).

The role of RAAS blockade in the development and progression of diabetic CKD over and above BP control needs reevaluation. Angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) are not able to prevent the development of microalbuminuria in normotensive individuals with either T1DM or T2DM (26,27) and their role in normotensive individuals with low levels of microalbuminuria is unclear. The relative benefits of ACE inhibitors vs. ARBs vs. direct renin inhibitors in T1DM and T2DM patients with hypertension and albuminuria remain to be determined. Similarly, the role of combinations of drugs acting in the RAAS remains controversial. Finally, whether RAAS blocking drugs have an effect over and above blood pressure reduction in decreasing the rate of CKD progression in those without increased AER is not clear.

Many other controversies exist in the management of diabetic CKD. Although statins likely decrease CVD in those with Stages I-IV CKD (28,29), proof that they are effective in patients on dialysis is lacking (30-32). Should statins be stopped when patients go on dialysis? Are there any data for other cholesterol-lowering medications in patients with diabetic CKD?
Another controversial issue is the use of metformin to control hyperglycemia in patients with decreased GFR. Although lactic acidosis is a potential problem in such patients, the risk appears to be small (33-35). Whether the current guidelines are too strict deserves a reanalysis.

To address these and other issues, KDIGO is conducting a Controversies Conference on Diabetic Kidney Disease. The conference will be held on 16-18 March, 2012 at a venue to be determined. Drs. Carl Erik Mogensen and Mark Molitch will co-chair this conference, which will attempt to define the current state of our knowledge in the management of diabetic kidney disease. Topic areas to be covered include: 1) epidemiology, 2) albuminuria, 3) glycemic control,4) RAAS blockade, 5) management of hypertension, and 6) role of statins.

Invited participants and speakers will comprise the leading worldwide experts in these topic areas, including nephrologists and diabetologists, to give the broadest views possible on the subject. Their task will be to summarize the existing knowledge, develop recommendations on what can be done to optimize the prognosis of patients diabetic kidney disease based on this knowledge, and to formulate and prioritize research questions. The conference output will include publication of a position statement.

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CONFERENCE AGENDA

Thursday, 15 March
20:00 – 22:00 hrs

LOCATION

20:00 – 22:00 hrs **Welcome Reception**

Day 1 – Friday, 16 March
08:00 – 17:30 hr

07:30 – 08:00 hrs **Continental Breakfast**

Introduction: Meeting Overview

08:00 – 08:10 hrs **Welcome and Introductions**
Presenters: Bertram Kasiske & David Wheeler, KDIGO Co-Chairs

08:10 - 08:20 hrs **Conference Overview and Objectives**
Presenters: Carl Erik Mogensen and Mark Molitch, Conference Co-Chairs

Plenary Sessions: Epidemiology of Diabetic Kidney Disease

Session Moderators: Carl Erik Mogensen and Mark Molitch

08:20 – 08:50 hrs **Global Epidemiology of DM in 2012**
Invited Presenter: William Herman

08:50 – 09:20 hrs **Advanced Renal Disease**
Invited Presenter: Eberhard Ritz

09:20 – 09:50 hrs **Cardiovascular Disease in DM**
Invited Presenter: Juliana Chan

Plenary Sessions: Albuminuria

Session Moderators: Carl Erik Mogensen and Mark Molitch

09:50 – 10:20 hrs **Pathogenesis of Albuminuria in DM**
Invited Presenter: Mark Cooper

10:20 – 10:50 hrs **Break**

10:50 – 11:20 hrs **Disease Progression: Albuminuria versus eGFR**
Invited Presenter: Richard MacIsaac

11:20 – 11:50 hrs **Albuminuria as a Target for Treatment**
Invited Presenter: Michel Marre

11:50 – 12:20 hrs **Multi-factorial Intervention, Early or Late?**
Invited Presenter: Peter Gæde

12:20 – 13:00 hrs **Lunch**

Plenary Sessions: Glycemic Control

Session Moderators: Carl Erik Mogensen and Mark Molitch

13:00 – 13:30 hrs **Type 2 Diabetes**
Invited Presenter: Amanda Adler

13:30 – 14:00 hrs **Type 1 Diabetes**
Invited Presenter: Mark Molitch

14:30 – 15:00 hrs **Break**

15:00 - 18:00 hrs **Breakout Sessions:**

Breakout Group #1: Evaluation and Albuminuria
Invited Discussion Leaders: Amanda Adler & Allan Flyvbjerg
(Room:)

Breakout Group #2: Glycemic Control
Invited Discussion Leaders: Robert Nelson and Wing Yee So
(Room:)

Breakout Group #3: Therapeutic Management
Invited Discussion Leaders: Dick de Zeeuw & Christoph Wanner
(Room:)

19:00 – 21:00 hrs **Group Dinner**

Day Two – Saturday, 17 March
8:00 to 18:30 hrs

LOCATION

07:30 - 08:00 hrs **Continental Breakfast**

Breakout Group Reports and Discussion

08:00 – 08:25 hrs **Breakout Group #1: Evaluation and Albuminuria**
Presenters: Amanda Adler & Allan Flyvbjerg

08:25 – 08:50 hrs **Breakout Group #2: Glycemic Control**
Presenters: Robert Nelson and Wing Yee So

08:50 – 09:15 hrs **Breakout Group #3: Therapeutic Management**
Presenters: Dick de Zeeuw & Christoph Wanner

Plenary Sessions: Hyperfiltration and Hypertension

Session Moderators: Carl Erik Mogensen and Mark Molitch

09:15 – 09:45 hrs **Hyperfiltration, the Earliest Renal Involvement in Diabetes, Type 1 and Type 2**
Invited Presenter: Piero Ruggenenti

09:45 – 10:15 hrs **Blood Pressure Target: CVD versus CKD**
Invited Presenter: Herman Haller

10:15 – 10:45 hrs **Break**

10:45 – 11:15 hrs **Combination Therapy**
Invited Presenter: George Bakris

11:15 – 11:45 hrs **Is Treatment Different in Type 1 vs Type 2 and When Should BP Therapy be Initiated?**
Invited Presenter: Per Løgstrup Poulsen

Plenary Sessions: RAAS Blockade

Session Moderators: Carl Erik Mogensen and Mark Molitch

11:45 – 12:15 hrs **Do we still think there is evidence for RAAS Blockade?**
Invited Presenter: Peter Rossing

12:15 – 12:45 hrs	**ACES vs ARBS** Invited Presenter: Johannes Mann
12:45 – 13:45 hrs	**Lunch**
13:45 – 14:15 hrs	**Is there a Role for Direct Renin Inhibitors?** Invited Presenter: Frederik Persson
14:15 – 14:45 hrs	**Statins** Invited Presenter: John Betteridge
14:45 – 15:15 hrs	**Metformin** Invited Presenter: Guntram Schernthaner
15:15 – 15:45 hrs	**Aspirin** Invited Presenter: Alberto Zanchetti
15:45 – 16:00 hrs	**Break**
16:00 – 18:30 hrs	**Breakout Sessions:** **Breakout Group #1: Evaluation and Albuminuria** **Invited Discussion Leaders: Amanda Adler & Allan Flyvbjerg** **(Room:)** **Breakout Group #2: Glycemic Control** **Invited Discussion Leaders: Robert Nelson and Wing Yee So** **(Room:)** **Breakout Group #3: Therapeutic Management** **Invited Discussion Leaders: Dick de Zeeuw & Christoph Wanner** **(Room:)**
20:00 – 22:00 hrs	**Group Dinner (Meet in hotel Lobby at 19:30 hrs)**

Day 3 - Sunday, 18 March
8:00 to 12:30 hrs

LOCATION

7:30 - 8:00 hrs **Continental Breakfast**

Breakout Group Reports and Discussion

08:00 – 08:30 hrs	**Breakout Group #1: Evaluation and Albuminuria** **Presenters: Amanda Adler & Allan Flyvbjerg**
08:30 – 09:00 hrs	**Breakout Group #2: Glycemic Control** **Presenters: Robert Nelson and Wing Yee So**
09:00 – 09:30 hrs	**Breakout Group #3: Therapeutic Management** **Presenters: Dick de Zeeuw & Christoph Wanner**
09:30 – 10:00 hrs	**Break/Check Out**
10:00 – 12:15 hrs	**Discussion and Consensus on Recommendations**
12:15 – 12:30 hrs	**Wrap up and next steps**
12:30 hrs	**Adjourn** (Departures)

Lunch available after adjournment