Primary outcomes of the Monitoring in Dialysis Study indicate that clinically significant arrhythmias are common in hemodialysis patients and related to dialytic cycle

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Sudden death is one of the more frequent causes of death for hemodialysis patients, but the underlying mechanisms, contribution of arrhythmia, and associations with serum chemistries or the dialysis procedure are incompletely understood. To study this, implantable loop recorders were utilized for continuous cardiac rhythm monitoring to detect clinically significant arrhythmias including sustained ventricular tachycardia, bradycardia, asystole, or symptomatic arrhythmias in hemodialysis patients over six months. Serum chemistries were tested pre- and post-dialysis at least weekly. Dialysis procedure data were collected at every session. Associations with clinically significant arrhythmias were assessed using negative binomial regression modeling. Sixty-six patients were implanted and 1678 events were recorded in 44 patients. The majority were bradycardias (1461), with 14 episodes of asystole and only one of sustained ventricular tachycardia. Atrial fibrillation, although not defined as clinically significant arrhythmias, was detected in 41% of patients. With thrice-weekly dialysis, the rate was highest during the first dialysis session of the week and was increased during the last 12 hours of each inter-dialytic interval, particularly the long interval. Among serum and dialytic parameters, only higher pre-dialysis serum sodium and dialysate calcium over 2.5 mEq/L were independently associated with clinically significant arrhythmias. Thus, clinically significant arrhythmias are common in hemodialysis patients, and bradycardia and asystole rather than ventricular tachycardia may be key causes of sudden death in hemodialysis patients. Associations with the temporal pattern of dialysis suggest that modification of current dialysis practices could reduce the incidence of sudden death.

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The high incidence of sudden death (SD) in end-stage renal disease (ESRD) is well described,[1–3] and SD is most likely after the 3-day inter-dialytic interval.[4–6] Other studies have shown that SD is increased with low potassium or calcium dialysis baths.[7,8] Although these observations suggest that thrice-weekly hemodialysis induces arrhythmia, the occurrence of atrial and ventricular arrhythmias during and between hemodialysis sessions is not well characterized.

The development of implantable, continuous cardiac monitoring devices (implantable loop recorders [ILRs]) has facilitated long-term monitoring of cardiac rhythm. Recent ILR studies have demonstrated a much higher than previously suspected incidence of occult atrial fibrillation among individuals with stroke,[9] confirming the potential of ILRs to assess arrhythmia burden in vulnerable populations. Hemodialysis patients represent a high-risk group in whom stringently characterizing events could provide critical benefits. We prospectively used ILR to assess arrhythmia burden in a multicenter cohort of hemodialysis patients during a long-term observation period in order to identify arrhythmia burden and type and characterize associations with the dialysis procedure.

RESULTS

Baseline demographics

Eighty-one patients were enrolled, and 66 were implanted with an ILR: 43 from the United States and 23 from India

(Figure 1). The ratio of screened to enrolled subjects was slightly higher in the United States than in India, but rates of ILR implantation in enrolled subjects and follow-up through 6 months were similar (Supplementary Figures S1 and S2). Mean age was 56 years, 70% were male, and 53% were African American (Table 1). Diabetes was the cause of ESRD in 42%, mean body mass index was 29, 70% had never smoked, 49% had ischemic heart disease, 26% had congestive heart failure, 14% had undergone coronary artery bypass surgery, and mean left ventricular ejection fraction (LVEF) was 56%. Only 3% had LVEF <35%.

Safety

There were 57 adverse events, 49 of which were serious (Supplementary Table S1). Only 1 (2%) serious adverse event was adjudicated as related to the implant procedure, relatedness was uncertain in 1 case (2%), and none were device-related.

Procedure-related adverse events ($n = 6$) included impaired wound healing (2 subjects), staphylococcal wound infection (1 subject), suture-related complication (1 subject), hematoma (1 subject), and symptomatic atrial fibrillation 6 days after insertion that was severe but resolved with therapy. Other events were of mild severity. There were 3 episodes of device-related chest or implant site pain. None were serious and each was of mild severity. Two resolved with appropriate treatment, and the third with device removal.

CSA and non-CSA arrhythmia incidence

During the 6-month study, 1678 instances of clinically significant arrhythmia (CSA) occurred (Table 2) in 44 of 66 subjects (67%). The majority (1461) were bradycardic events, which occurred in 13 subjects (20%). There were an additional 14 asystolic episodes in 6 subjects (9%). Five patients had pacemakers inserted in response to CSA. Two of 3 patients with pacemaker insertion prior to 6 months had their ILR explanted. The third had pacemaker insertion at 1.4 months and was continued in the study in order to capture arrhythmias not responsive to pacing or that could be

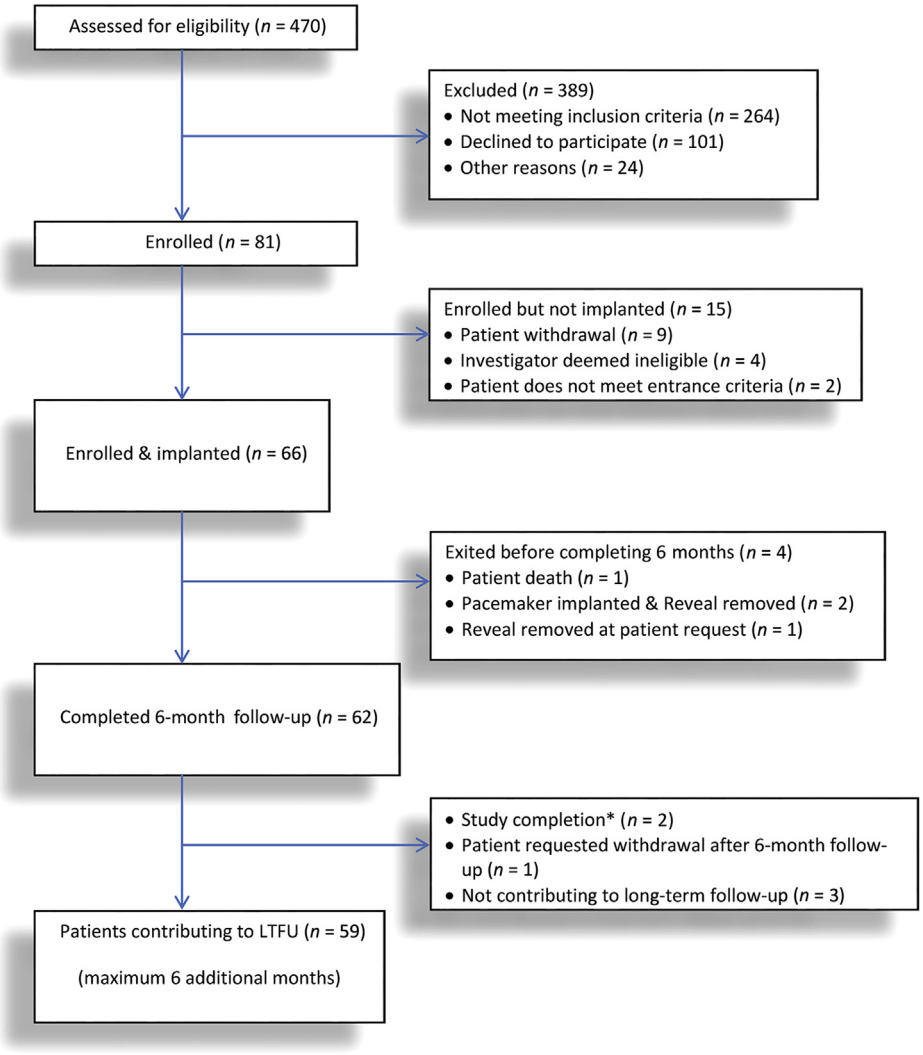

Figure 1 | Flow of patients in the Monitoring in Dialysis (MiD) trial. *Study was complete when last implanted patient completed 6 months of follow-up. LTFU, long-term follow-up.