My one and noble heart has witnesses
In all love’s countries, that will watch
awake;
And when blind sleep falls on the spying
senses,
The heart is sensual, though five eyes
break.

DYLAN THOMAS

“When all my five &
country senses see”
Cardiac disease, as noted in past USRDS Annual Data Reports, remains the single largest cause of mortality in the ESRD population. The burden of cardiovascular morbidity and mortality in patients with chronic kidney disease, however, is not restricted to the ESRD population. It has become increasingly apparent that the presence of severe chronic kidney disease is not only a powerful independent prognostic factor for the prediction of cardiovascular morbidity and mortality, but also a “multiplier” for the risk of death.

The research mandate of the USRDS for the past years has been broadened to include studies focusing on patients with severe chronic kidney disease who are not receiving renal replacement therapy. This focus is mirrored here in the 2005 chapter by the Cardiovascular Special Studies Center, with detailed data provided on the comparison of parallel outcomes in patients with dialysis-dependent ESRD, CKD patients in the general Medicare population, and general Medicare patients without CKD identified from claims data.

Although the dialysis population has been rightfully identified as a population at extraordinary risk for cardiovascular disease, the conceptual importance of CKD as a marker for high cardiovascular risk in the general Medicare population should not be underestimated. While the risk of cardiovascular morbidity and mortality in the general Medicare population is lower than that of the dialysis population, when viewed from the perspective of younger patients with cardiovascular disease, the general Medicare population is rightly considered a high-risk population in its own right.

There are three major themes in this chapter. The first, illustrated in Figure 9.1, details the importance of age, diabetes as the primary cause of ESRD, and the presence of CVD at the time of dialysis initiation as they relate to survival. Clearly, all dialysis patients do not have equivalent outcomes. One issue, raised by clinical trialists designing interventional studies in dialysis patients, is the absence of datasets that include crucial data on prior cardiovascular morbidity at the time of dialysis initiation. Although the Medical Evidence form underestimates the burden of comorbid cardiovascular disease, these data show the important interaction of age, diabetes, and comorbid cardiovascular disease on survival.

Coronary revascularization procedures, both percutaneous and surgical, are a cornerstone of therapy for ischemic heart disease. In keeping with the USRDS focus on the spectrum of CKD (including ESRD), this chapter highlights the epidemiology and outcomes of coronary revascularization in incident and prevalent dialysis patients. One theme is the parallel comparison of hemodialysis to peritoneal dialysis patients. Figure 9.2 displays the demographics of the entire incident population, while Figure 9.3 contrasts the prevalence of cardiovascular comorbidity at the time of dialysis initiation.
for the two modalities. As shown in Figure 9.3, congestive heart failure is more common in hemodialysis patients at initiation (33 percent), compared to 23 percent of peritoneal dialysis patients. Figures 9.4–5 contrast procedure use by dialysis modality for incident patients (9.4) and survival after revascularization by modality and diabetic status for incident patients (9.5).

The next spread focuses on prevalent patients. Figures 9.12–13 show the rate of procedure utilization and survival after revascularization in prevalent hemodialysis and peritoneal dialysis patients. As shown in Figure 9.13, older age is associated with increased mortality after coronary revascularization. Figures 9.11, 9.14, and 9.15 contrast mortality after revascularization in the dialysis population, general Medicare patients with CKD, and general Medicare patients without CKD.

The last spread addresses a relatively neglected cardiovascular problem in dialysis patients: the epidemiology of atrial fibrillation and stroke. As shown in Figure 9.17, atrial fibrillation is a common clinical problem in dialysis patients, yet it has not generated the same degree of research interest as issues relating to ischemic heart disease in ESRD patients. The main purpose of this spread is to provide a broad overview of the current epidemiology of atrial fibrillation and stroke in dialysis patients as a stimulus for more detailed observational studies. Ideally, observational studies on atrial fibrillation would be used for the subsequent design of clinical trials.

We have attempted to present an overview on two very distinct cardiovascular topics of interest: coronary revascularization and atrial fibrillation. It is the aim of the Cardiovascular SSC that this chapter should help stimulate further research studies and, ultimately, clinical trials, as the techniques for both percutaneous (e.g., drug eluting stents) and surgical coronary revascularization (e.g., off-pump procedures) have been refined over time. It is critical that optimal therapies for revascularization become available for the high-risk populations detailed in this chapter.

A logical outcome of this observational work would thus be a clinical trial comparing the efficacy of surgical to percutaneous coronary revascularization procedures in patients with varying degrees of CKD, including ESRD. As noted above, there is also more to be learned about the optimal treatment of atrial fibrillation in dialysis patients. The Cardiovascular SSC hopes that both of these ends will be furthered by this chapter.

**Chapter Highlights**

- **Figure 9.1** After initiation of dialysis, survival is related to age, diabetic status, and presence of comorbid cardiovascular disease. **Figure 9.5** Diabetic peritoneal dialysis patients have a higher rate of death following coronary revascularization than non-diabetics. **Figure 9.9** Since 1995, there has been an increased use of coronary stenting as a method of coronary revascularization. **Figure 9.12** Surgical revascularization is associated with a subsequent decline in the death rate, while percutaneous coronary intervention has a more relative uniform mortality hazard over time. **Figure 9.14** CKD appears to be associated with a higher mortality rate than diabetes. **Figure 9.20** The overall stroke rate is higher in patients with AF, and this appears to be attributable to ischemic stroke.
figures 9.2–15 show data on the demographics of the entire incident dialysis population during incident years 1995–2003. At dialysis initiation, the main difference between hemodialysis and peritoneal dialysis patients is the higher prevalence of congestive heart failure as a comorbid cardiovascular condition—33 percent for hemodialysis patients and 23 percent for peritoneal dialysis patients in 2003.

Figures 9.4–5 show procedure utilization rates in incident hemodialysis and peritoneal dialysis patients, and survival following coronary revascularization procedures. As shown in Figure 9.4, the rate of coronary stent utilization exceeds that for other types of coronary revascularization procedures (mirroring the trend in the general population). Although ischemic heart disease is common in dialysis patients, the overall utilization rate of coronary revascularization procedures actually remains low. There has been a striking increase in the first-year procedure rate for coronary stents, with the rate tripling from approximately 10 per 1,000 patient years in 1995–1997 to 30 in 2001–2003. As shown, however, most patients do not receive coronary revascularization procedures.

Figure 9.5 contrasts, by diabetic status, death rates and survival probabilities for incident hemodialysis and peritoneal dialysis patients undergoing coronary revascularization procedures. Diabetic peritoneal dialysis patients have the highest mortality after coronary revascularization, with a three-year survival of approximately 22 percent after coronary bypass surgery, and 17 percent after coronary stenting. Two-year survival after coronary bypass surgery is only 37 percent for diabetics on this modality, and 47 percent for non-diabetics, in contrast to 50 and 53 percent, respectively, for patients on hemodialysis.

Coronary stenting has rapidly supplanted balloon angioplasty as the primary mode of percutaneous coronary revascularization in the U.S. In the incident hemodialysis population, two-year survival after this procedure is 47 and 53 percent for those with and without diabetes, respectively—in contrast to 31 and 46 percent for those on peritoneal dialysis.

{Figures 9.2–3} incident dialysis patients, age 20 & older. Comorbidities identified from the Medical Evidence form. {Figure 9.4} incident dialysis patients, age 20 & older; adjusted for age, gender, race, & primary diagnosis. Long-term procedure use examined for 1998–2000 cohort. {Figure 9.5} incident dialysis patients, age 20 & older; adjusted for age, gender, race, & primary diagnosis. Cohort year is defined based on year of procedure. Long-term survival following procedure examined for 1998–2000 cohort.
Coronary revascularization in prevalent patients

9.6 Demographics of the prevalent population

Dialysis: Age

- Female: 65-74
- Male: 65-74

Gender

- Female: 65-74
- Male: 65-74

Race

- Other: 65-74
- Asian: 65-74
- Native American: 65-74
- Black: 65-74
- White: 65-74

Diabetic status

- Diabetic: 65-74

9.7 Comorbidity in prevalent patients

Dialysis

- General Medicare with CKD
- General Medicare without CKD

9.8 Geographic variations in coronary revascularization rates, per 1,000 patient years at risk, by state & HSA

General Medicare: CKD, CABG

- 8.47 + (11.66)
- 6.91 to <8.47
- 6.43 to <6.91
- Insuff. data

General Medicare: No CKD, CABG

- 8.47 + (N/A)
- 6.91 to <8.47
- 6.43 to <6.91

General Medicare: CKD, Stent

- 13.4 + (17.8)
- 12.2 to <13.4
- 10.9 to <12.2
- Insuff. data

General Medicare: No CKD, Stent

- 13.4 + (NA)
- 12.2 to <13.4
- 10.9 to <12.2

Dialysis population: CABG

- 16.4 + (18.3)
- 15.2 to <16.4
- 14.0 to <15.2
- 12.5 to <14.0
- 12.5 to <14.0

Dialysis population: Stent

- 27.2 + (32.0)
- 24.3 to <27.2
- 21.9 to <24.3
- 18.9 to <21.9
- 18.9 to <21.9
The prevalent dialysis and general Medicare CKD populations both have nearly equal distributions of men and women, of general Medicare patients without CKD, in contrast, only 40 percent are male (Figure 9.6). This implies that the survival advantage normally associated with female gender is in part nullified by the presence of severe CKD, and is likely related to other factors as well, including the varying distribution of diabetes—in 2003, present in 57 percent of the dialysis population and 45 percent of general Medicare patients with CKD, but only 17 percent of general Medicare patients without CKD.

Patients with CKD have a higher coronary revascularization rate, yet most do not receive coronary revascularization procedures (Figure 9.9). For all groups shown, the largest increase in first-year procedure rates since 1995 has occurred for coronary stenting—from two per 1,000 patient years to 30 in dialysis patients, from two to 17 in general Medicare patients with CKD, and from 1.3 to 10 in those without CKD. Not surprisingly, there has been a decline in the rate of angioplasty without stenting.

Clearly, the main expansion in the use of coronary revascularization procedures has occurred in patients receiving coronary stents. Similar findings are obtained when comparing the procedure utilization rates in prevalent hemodialysis and peritoneal dialysis patients. In these prevalent patients, there is about a 7 percent cumulative probability of receiving a stent for a hemodialysis patient and 8 percent at three years for a peritoneal dialysis patient. In both groups there has been a marked increase in coronary stent utilization from 1995 to 2003.

( Figures 9.6–7) dialysis: January 1 point prevalent dialysis patients, age 20 & older, & on dialysis for at least one year. General Medicare (5 percent sample): January 1 point prevalent patients, age 66 & older, & enrolled in Medicare for at least one year. Comorbidities identified from Medicare Parts A & B claims. For dialysis patients, comorbidities also identified from the Medical Evidence Form. (Figure 9.8) per 1,000 patient years at risk; period prevalent Medicare dialysis patients age 20 & older, by HSA, unadjusted; period prevalent general Medicare population (5 percent sample) age 66 & older, 1998–2000, by state, unadjusted. (Figure 9.9) January 1 point prevalent dialysis patients (includes those with unknown dialysis modality), & general Medicare patients (5 percent sample), age 66 & older; adjusted for age, gender, & race. Long-term procedure use examined for 2001 cohort. ( Figure 9.10) January 1 point prevalent dialysis patients, age 20 & older; adjusted for age, gender, race, & diabetic status. Long-term procedure use examined for 2001 cohort.
Survival following revascularization in prevalent patients

Patients with more severe CKD have a higher death rate and worse survival after all types of coronary revascularization (Figure 9.11). In all patient groups, the death rate is highest in the first year after revascularization, but the comparison across groups at two years is particularly noteworthy. For Medicare patients without CKD, for those with CKD, and for dialysis patients age 66 and older, respectively, two-year survival after coronary bypass surgery is 86, 63, and 40 percent—markedly worse as disease severity increases. Two-year survival after angioplasty is 86, 71, and 36 percent, and after coronary stents it is 88, 69, and 38 percent.

Age, not surprisingly, is a powerful predictor of all-cause mortality, as illustrated in Figures 9.12–13. Adjusted survival is somewhat better in hemodialysis patients than in their peers on peritoneal dialysis. Two-year survival after bypass surgery in patients younger than 65, for example, is 55 and 50 percent for hemodialysis and peritoneal dialysis, respectively; following a stent it is 58 and 49 percent. In patients 65 or older the difference is larger, with 42 percent of hemodialysis patients surviving two years, compared to 28 percent of those on peritoneal dialysis. Comparisons by modality, however, require caution, as the patient groups may not be comparable over time due to such factors as differential rate of transplantation (i.e. “informative censoring”), which may impact their clinical characteristics over time.

Figures 9.14–15 show the influence of diabetes on death rates and survival probabilities after revascularization. After coronary bypass surgery, two-year survival for diabetic patients is 86 percent in the general Medicare population without CKD, compared to 66 percent for general Medicare patients with CKD and 38 percent for dialysis patients age 66 and older; among non-diabetic patients, survival is 87 (surprisingly similar to the non-CKD population), 59, and 43 percent, respectively. These adjusted survival data suggest that CKD has a greater impact on mortality after revascularization then would be attributed to diabetic status.

Not unexpectedly, surgical coronary revascularization is associated with a higher early hazard of peri-procedural death than percutaneous coronary intervention. For this reason, comparisons across revascularization groups are significantly affected by the length of followup after the revascularization procedure. Note the striking difference in death rates occurring after varying time intervals. In the first 12 months after coronary revascularization, for example, the death rate is 113 per 1,000 patient years for non-CKD general Medicare patients, 301 for general Medicare CKD patients, and 614 for dialysis patients age 66 or older. At 36 months the rate significantly declines—to 60, 112, and 316, respectively. For dialysis patients receiving coronary stents, the death rate is 611 at one year, and 546 at three years. If clinical trials comparing surgical to percutaneous coronary intervention in patients with severe CKD are planned, the length of followup time will be a critical variable, as mortality rates are not constant during followup. The mortality hazard associated with each revascularization procedure has a different temporal pattern, which could significantly affect the results of a comparative clinical trial.

### Figures 9.11 & 9.14–15

Prevalent dialysis patients & general Medicare patients (5 percent sample) receiving their first coronary revascularization procedure during 1995–2002, on dialysis or enrolled in Medicare for at least one year, & age 66 & older. Adjusted for age, gender, race, & diabetic status (Figure 9.11), & for age, gender, & race (Figures 9.14–15). Long-term survival following procedure examined using 2001 cohort. For Figure 9.11, angioplasty mortality rates available only for 1st year. (Figures 9.12–13) Prevalent dialysis patients age 20 & older, receiving their first coronary revascularization procedure during 1995–2002 & on dialysis for at least one year; adjusted for age, gender, race, & diabetic status. Long-term survival following procedure examined using 2001 cohort.
In this spread we provide an overview of the epidemiology of atrial fibrillation (AF) and stroke in dialysis patients. In 2003, 36 percent of AF patients were age 75 or older, compared to only 20 percent of dialysis patients overall (Figure 9.16). Gender distributions are similar, but there is a marked difference in the racial distribution—67 percent of AF patients are white, compared to 52 percent of the dialysis population.

In 2003, 13 percent of point prevalent hemodialysis patients had a reported prevalence of AF, versus 7 percent of those on peritoneal dialysis; the incidence of AF was 9 and 7 percent, respectively (Figure 9.17). Both incident and prevalent AF are associated with excess mortality (Figure 9.18). Among prevalent dialysis patients in 2002, the death rate was 485 per 1,000 patient years for those with incident AF—2.3 times greater than the rate of 213 in those without AF. Similarly, the mortality rate for patients with prevalent AF was 480 per 1,000 patient years versus 213 for those without it. Since AF may be associated with other types of serious cardiac comorbidity, this does not imply that the mortality hazard can be directly attributed to AF, as the marked difference in mortality may reflect the presence of other serious linked cardiovascular comorbid conditions.

Figure 9.19 shows the geographic distribution, by state, of incident and prevalent AF. These maps are somewhat surprising, as the percent of dialysis patients with AF appears to be lowest in the southern states. The next figures deal with the association of AF and stroke. In 2002, the rate of all strokes was 64 per 1,000 patient years in dialysis patients with AF, and 40 in those without it (Figure 9.20). As expected, this difference is attributable to the rate of ischemic stroke, as rates of hemorrhagic stroke are comparable over the decade. There is no significant difference in the time to hemorrhagic stroke, but an apparent difference for time to ischemic stroke (Figure 9.21). At one year, 3 percent of non-AF patients have an ischemic stroke compared to 5 percent of those with identified AF. Obviously, a longer followup time is of interest for estimating the long-term hazard of stroke attributable to AF. There does not appear to be a significant difference related to dialysis modality and risk of ischemic stroke in patients with atrial fibrillation (Figure 9.22).

Data presented here should be viewed as an overview of the epidemiology of AF and stroke in dialysis patients. The major finding is the two-fold risk of death, and...
the 50 percent increased rate of stroke, associated with AF. These data suggest that further studies, including both observational and clinical trials, may be warranted in dialysis patients with AF.

[Figure 9.16] point prevalent dialysis patients who remain alive, on the same modality, & with Medicare as primary payor for the entire calendar year. AF identified from claims during the calendar year. [Figure 9.17] point prevalent dialysis patients alive, on the same modality, & with Medicare as primary payor for the entire calendar year. AF identified from claims during the calendar year. Incidence defined as the percent of patients without AF in 2002 who are identified through claims as having AF during 2003. [Figures 9.20-23] point prevalent dialysis patients who remain alive, on the same modality, & with Medicare as primary payor for the entire calendar year. Figures 9.21-23 use the 2002 cohort, with stroke identified in 2003, in which incidence is identified, or two years after the original cohort year. [Figure 9.19] point prevalent dialysis patients, 2002, who remain alive, on their same modality, & with Medicare as primary payor for all of 2002. AF identified from claims during 2002. Incidence is defined as the percent of patients without AF in 2002 who are identified through claims as having AF during 2003. [Figures 9.20-23] point prevalent dialysis patients who remain alive, on the same modality, & with Medicare as primary payor for all of 2002. AF identified from claims during 2002. Includes patients who had an inpatient claim with a stroke as any diagnosis at any point during 2003 prior to death, change of modality, change of payor status, or December 31, 2003.

### Geographic variations in rates of stroke in patients with & without atrial fibrillation, by state

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<th>Non-AFIB</th>
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With atrial fibrillation Without atrial fibrillation

- 59.9 to <77.9
- 31.0 to 46.0
- 55.5 to 59.9
- 46.0 to 55.5
- Insuff. data

- 59.9 to <60.1
- 31.0 to <46.0
- 55.5 to <59.9
- 46.0 to <55.5
Figure 9.1 After initiation of dialysis, survival is related to age, diabetic status, and presence of comorbid cardiovascular disease.

Figure 9.2 The incident hemodialysis population tends to be older, with a larger proportion of white patients, than the incident peritoneal dialysis population. Figure 9.3 There is a higher occurrence of comorbid congestive heart failure in hemodialysis versus peritoneal dialysis patients at dialysis initiation. Figure 9.4 Most incident dialysis patients do not receive coronary revascularization procedures in the three years following dialysis initiation. The probability of receiving coronary revascularization is comparable for hemodialysis and peritoneal dialysis patients. Figure 9.5 Diabetic peritoneal dialysis patients have a higher rate of death following coronary revascularization than non-diabetics.

Figure 9.6 The proportion of black patients is much larger in the dialysis population than in the general Medicare population. There are proportionally more women in the general Medicare non-CKD population. Figure 9.7 Chronic kidney disease is characterized by a high prevalence of comorbid cardiovascular disease. Figure 9.9 There has been an increased use of coronary stenting as a method of coronary revascularization over time (1995–2003) in dialysis patients, general Medicare CKD patients, and general Medicare non-CKD patients. In contrast, utilization of surgical revascularization has been relatively unchanged. Figure 9.10 The pattern of coronary revascularization use is similar in peritoneal dialysis and hemodialysis patients. There has been a marked increase since 1995 in the use of coronary stents, and little change in the use of surgical revascularization.

Figure 9.11 There is a significant difference in the pattern of mortality after surgical versus percutaneous coronary intervention. Surgical revascularization is associated with a subsequent decline in the death rate, while percutaneous coronary intervention has a more relative uniform mortality hazard over time. Figures 9.12–15 Older age and diabetes are associated with increased mortality after coronary revascularization. Chronic kidney disease, however, appears to be associated with a higher mortality rate than diabetes.

Figure 9.16 Prevalent patients with atrial fibrillation (AF) are demographically older, and have a larger relative proportion of white patients compared to the general dialysis population. Figure 9.18 There is a two-fold mortality risk associated with AF. Figure 9.19 At a state level, the percent of patients with AF appears to be lower in the southern states. Figure 9.20 The overall stroke rate is higher in patients with AF, and this appears to be attributable to ischemic stroke. Figure 9.21 Among patients with AF, 5 percent are identified as having an ischemic stroke within the first year versus 3 percent in those without AF. Figure 9.22 Time to first stroke in AF patients does not appear to be related to dialysis modality.

MAPS: NATIONAL MEANS & PATIENT POPULATIONS

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