Most Important Outcomes Research Papers in Cardiovascular Disease in the Elderly

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The following are highlights from the new series, *Circulation: Cardiovascular Quality and Outcomes* Topic Review. This series will summarize the most important manuscripts, as selected by the Editor, that have published in the *Circulation* portfolio. The objective of this new series is to provide our readership with a timely, comprehensive selection of important papers that are relevant to the quality and outcomes and general cardiology audience. The studies included in this article represent the most significant research in the area of cardiovascular disease in the elderly. (*Circ Cardiovasc Qual Outcomes*. 2012;5:e17-e26.)

Our society is aging. The number of Americans older than 65 years of age is expected to increase from 13% in 2000 to 20% by 2030 as the baby boomers enter their senior years.[1] By 2050, the number above the age of 85 years is expected to triple. The practice of cardiology has become entwined with geriatric medicine.

Yet, despite these trends, our understanding of cardiovascular disease in older persons is still in many cases rudimentary. This may not be surprising, as the elderly are poorly represented in clinical research. Historically, patients older than the age of 65 years were often excluded from clinical trials. Those over the age of 85 years are still rarely included. In addition, patients with common comorbidities found in older persons such as chronic kidney disease, anemia, chronic obstructive pulmonary disease, and cognitive impairment are often intentionally kept out of clinical investigations.

Moreover, models of care are rarely optimized for older persons.[2] Too often, care for vulnerable elders is procedure-based and fragmented rather than integrated and continuous with involvement of both patients and caregivers. Comorbidities, geriatric syndromes, and polypharmacy are often ignored when making treatment decisions. Quality of life, symptom palliation, and other patient-centered outcomes are often deemphasized in favor of surrogate markers and targets that are easier to measure but may not accurately reflect underlying patient risk or goals of care.

It is for these reasons that we are dedicating the topic summaries within this issue of *Circulation: Cardiovascular Quality and Outcomes* to cardiovascular disease in older persons. We have included studies relating cardiovascular risk to clinical syndromes often found in older persons such as frailty and heart failure with preserved ejection fraction. We have also included research on important nonpharmacologic interventions in the elderly such as exercise as well as commonly performed invasive procedures such as implantable cardioverter-defibrillator placement, percutaneous coronary intervention, and, increasingly, transcatheter aortic valve replacement. Last, we have incorporated studies that examine hospital and health system performance for older persons with heart failure, acute myocardial infarction, and stroke.

We hope you find these reviews useful, and we welcome your feedback as we try to best meet the needs of our readership.

Age-Related Differences in Characteristics, Performance Measures, Treatment Trends, and Outcomes in Patients With Ischemic Stroke

Summary: Prior studies have demonstrated lower use of guideline-recommended therapy and worse poststroke outcomes in older patients. The aim of this study was to evaluate temporal changes in adherence to performance measures and early clinical outcomes among acute ischemic stroke patients in the Get With The Guidelines (GWTG) program. The authors identified 502 036 ischemic stroke admissions among 1256 hospitals from 2003 to 2009. Data were analyzed by the following age groups: <50, 50 to 59, 60 to 69, 70 to 79, 80 to 89, and ≥90 years. Seven predefined performance measures relating to intravenous tissue plasminogen activator, antithrombotic medication, deep venous thrombosis prophylaxis, and other areas were analyzed. Mean age of ischemic stroke patients was 71 years; 52.5% were women. Although older patients (≥90 years) were less likely to be discharged home (42.1%) and more likely to die in the hospital (10.3%) compared with younger patients (<50 years), there were substantial temporal improvements in performance measures from 2003 to 2009 for each age group, and many age-related treatment gaps were narrowed or eliminated over time.

Conclusion: Study results are encouraging because they demonstrate significant improvement in the standard of care for acute ischemic stroke patients across the United States. Improvements in performance metrics were more frequently observed in older patients and resulted in narrowing of age-related treatment gaps. However, most of the hospitals participating in the GWTG-Stroke program are self-selected and probably have more interest in quality improvement, thereby challenging the generalizability of the results to the entire nation.[3]

Exercise Capacity and Mortality in Older Men: A 20-Year Follow-Up Study

Summary: Regular exercise is associated with improved life quality and survival in young and middle-aged subjects. Much less is known, however, about the effects of exercise in the elderly. The authors examined the association between physical fitness and mortality rates among 5314 elderly male veterans aged 65 to 92 years. Physical

fitness categories were established on the basis of peak metabolic equivalents (METs), estimated from symptom-limited exercise tolerance testing. Over a median follow-up time of 8.1 years, 2137 patients died. Baseline exercise capacity was higher among survivors (6.3±2.4 METs versus 5.3±2.0 METs, *P*<0.001). Exercise capacity was a strong predictor of mortality, with ≈13% lower risk for each 1-MET increase in exercise capacity. The results were stable after adjustment for a host of variables including age, body mass index, cardiovascular risk factors, and cardiovascular medications.

Conclusion: This study demonstrates that higher exercise capacity predicts lower all-cause mortality among the elderly. The findings remained consistent after multivariable adjustment and a variety of sensitivity analyses. Nevertheless, as the authors expressed, it is not known to what extent exercise capacity reflects physical activity patterns. In addition, it remains unclear whether the link between exercise capacity and outcomes is causal, especially as interventions aimed at improving exercise capacity[4] have not regularly conferred the anticipated magnitude of benefits seen in large observational databases such as this.[5]

Cystatin C and Sudden Cardiac Death Risk in the Elderly

Summary: Sudden cardiac death (SCD) has been associated with moderate kidney dysfunction in patients with cardiovascular disease. The authors sought to determine whether SCD incidence was independently associated with measurement of impaired kidney function, using standard creatinine-based estimated glomerular filtration rate (eGFR) or levels of cystatin C. Serum levels of cystatin C and creatinine were evaluated from 4465 participants from the Cardiovascular Health Study without prevalent cardiovascular disease at baseline. The association between cystatin C tertiles and SCD was determined, using a multivariate Cox proportional hazards model. The authors also defined 3 groups of patients using both cystatin C–based and creatinine-based eGFR measurements: normal kidney function, preclinical kidney disease, and chronic kidney disease. Over the median follow-up period of 11.2 years, 91 SCD events were reported. The annual incidence of SCD events increased across cystatin C tertiles: 10, 25, and 32 events per 10 000 person-years in tertiles 1, 2, and 3, respectively. These associations persisted after multivariate adjustment. In comparison, the rate of SCD increased in a linear distribution across creatinine-based eGFR tertiles: 15, 22, and 27 events per 10 000 person-years in tertiles 1, 2, and 3, respectively. However, after multivariate adjustment, no significant associations remained between creatinine-based eGFR and SCD. After excluding persons with chronic kidney disease, participants with preclinical kidney disease had a 2-fold SCD risk compared with those without chronic kidney disease.

Conclusion: The results show an association between impaired kidney function, as measured by cystatin C, and the risk of SCD that is independent of patient demographics, traditional cardiovascular risk factors, and use of common cardiac medications among ambulatory elderly in the community without clinical cardiovascular disease at baseline. While an association between chronic kidney disease and SCD has been described in the literature, this study extends the risk of SCD to the setting of preclinical kidney disease, as many persons with elevated cystatin C levels had normal serum creatinine. This study adds to the literature showing the relative superiority of cystatin C compared with creatinine as a marker of risk.[6–8]

National Patterns of Risk-Standardized Mortality and Readmission for Acute Myocardial Infarction and Heart Failure: Update on Publicly Reported Outcomes Measures Based on the 2010 Release

Summary: The Centers for Medicare and Medicaid Services (CMS) publicly report hospital 30-day risk-standardized mortality rates

(RSMRs) and risk-standardized readmission rates (RSRRs) for patients hospitalized with acute myocardial infarction (AMI) and heart failure (HF). RSMRs and RSRRs are calculated using hierarchical logistic modeling to account for patient clustering by hospital and are risk-standardized for age, sex, and comorbidities. The authors provided a national perspective on hospital performance for the 2010 release of these measures. Between July 1, 2006, and June 30, 2009, median RSMR for AMI was 16% (range, 10.3% to 24.6%; absolute difference, 5.2% for hospitals between the 5th and 95th percentiles) and median RSMR for HF was 10.8% (range, 6.6% to 18.2%; absolute difference of 5.0% between the 5th and 95th percentiles). Median RSRR for AMI was 19.9% (range, 15.3% to 26.3%; absolute difference, 3.9% between the 5th and 95th percentiles) and median RSRR for HF was 24.5% (range, 17.3% to 32.4%; absolute difference, 6.7% between the 5th and 95th percentiles). Compared with the previous reporting period, a small percentage of hospitals had either significantly improved or worsened RSMRs or RSRRs for HF, AMI, or both conditions.

Conclusion: Clinically meaningful variation exists for both RSMRs and RSRRs for HF and AMI. This variation suggests that many adverse events could be averted if performance moved toward what is being achieved by the top performing institutions in the United States. As some hospitals demonstrated substantial reductions in RSMRs or RSRRs as compared with the previous reporting period, significant improvement in hospital performance is possible.[9]

Incidence and Prevalence of Atrial Fibrillation and Associated Mortality Among Medicare Beneficiaries, 1993 to 2007

Summary: Atrial fibrillation (AF) is a common problem among older persons and is associated with considerable morbidity and mortality. In this study, the authors measured annual incidence and prevalence of AF and mortality after an AF diagnosis in 433 123 Medicare beneficiaries aged 65 years and older who were diagnosed with AF between 1993 and 2007. The incidence of AF remained steady during the 14-year study period, ranging from 27.3 to 28.3 per 1000 person-years. Higher incidence rates were found among men and white beneficiaries. The prevalence of AF increased in all age groups throughout the entire study period (mean, 5% per year). Mortality after AF diagnosis declined slightly over time but remained high. In 2007, the age- and sex-adjusted mortality rates were 11% at 30 days and 25% at 1 year.

Conclusion: Older patients with AF are at surprisingly high risk for mortality within 1 year of diagnosis, with approximately one-quarter dying within this time period. As previous research has demonstrated, the major source of morbidity and mortality among patients with AF is the combination of other cardiovascular conditions besides AF as well as noncardiovascular comorbidities.[10] Older patients with AF may therefore benefit from significant attention not only to their AF but also to other commonly associated cardiovascular and noncardiovascular conditions that drive a significant percentage of adverse outcomes in this population.[11]

Linking the National Cardiovascular Data Registry CathPCI Registry With Medicare Claims Data: Validation of a Longitudinal Cohort of Elderly Patients Undergoing Cardiac Catheterization

Summary: This study assessed the degree to which the cohort derived by linking the National Cardiovascular Data Registry's (NCDR) CathPCI Registry with the longitudinal Centers for Medicare and Medicaid (CMS) claims database, using indirect patient identifiers is representative of the overall CathPCI and CMS percutaneous coronary intervention (PCI) populations. From 2004 to 2006, 1492 hospitals filed CMS PCI claims and 663 hospitals contributed to CathPCI. Of these hospitals, 643 (97%) were linked across both data sources. Compared with all CMS PCI hospitals, the

linked data set contained fewer governmental, northeastern, southern, and low-volume (<200 beds) sites. Of the 993 351 CMS beneficiaries receiving PCI, 398 508 (40.1%) were found at centers in the linked database. Of these patients, 341 916 (86%) were linked to CathPCI Registry records. Linked and unlinked CMS patients had similar demographic and clinical features. In CathPCI, 477 456 elderly patients underwent PCI; 359 077 (75%) were able to be linked to CMS claims. Linked and unlinked CathPCI patients were mostly similar with the exception of fewer patients having commercial or health maintenance organization insurance in the linked cohort.

Conclusion: This Methods paper provides a description of a database that will be well positioned to study cardiovascular disease in the elderly. Using deterministic matching, the authors were able to build a dataset that was representative of the elderly population undergoing PCI. This linked dataset is valuable because it leverages the extensive patient-level clinical information from CathPCI and the capacity for long-term follow-up with CMS data. This linkage should allow investigators to conduct comparative effectiveness studies that were previously not possible.[12]

Frailty and Cardiovascular Disease

Chronological age does not always reflect biological status, which may vary from robust to frail. This concept of "frailty" among older patients with cardiovascular disease has emerged primarily from the geriatrics literature, where frailty is considered a biological state characterized by increased vulnerability and decreased resistance to physiological stressors.[13–15] From a syndromic perspective, frailty is associated with loss of skeletal muscle mass, weight loss, reduced walking speed, exhaustion, and reduced activity.[13] In recent years, this concept of frailty has been applied to patients presenting with acute cardiac illness as well as those undergoing procedural interventions such as cardiac surgery. Through these studies, it has been shown that frailty provides additional short- and long-term prognostic information above and beyond traditional demographic information and medical comorbidities.

Frail Patients Are at Increased Risk for Mortality and Prolonged Institutional Care After Cardiac Surgery

Summary: As the number of older frail patients undergoing cardiac surgery increases, the authors sought to determine if frailty was a risk factor for postprocedural adverse outcomes. The authors identified 3826 patients at a single center undergoing cardiac surgery and prospectively collected information on patients' activities of daily living (Katz index), ambulation status (completely independent versus requiring assistive device), and history of physician-documented dementia; 4.1% of patients had abnormalities in at least 1 of these 3 categories and were considered to be frail. Frail patients were older, had greater comorbidity burden, were more likely to present with acute disease, and were more likely to require more complex operative procedures. By logistic regression, frailty was an independent predictor of in-hospital mortality (odds ratio, 1.8), reduced survival at 2 years (odds ratio, 1.5), and discharge to an institution (odds ratio, 6.3).

Conclusion: As a concept, frailty has been defined in multiple ways. Here, frailty seems to be described primarily in terms of disability, meaning difficulty with carrying out functional tasks (activity of daily living impairment, difficulty with ambulation). Nonetheless, this characterization of preoperative frailty produced similar results with previous data showing increased hospitalization, mortality, and institutionalization among frail community-dwelling populations where frailty was defined in an alternate manner.[14] Perhaps the most striking result from this study was that frail operative patients had a 6 times higher odds of being discharged to a nursing facility. Both patients and providers should be aware of this information before proceeding with surgery, as the requirement for institutionalization may in some cases be permanent.[16]

Frailty Is Independently Associated With Short-Term Outcomes for Elderly Patients With Non–ST-Segment Elevation–Myocardial Infarction

Summary: The authors prospectively examined the influence of frailty on 1-month outcomes after non–ST-elevation–myocardial infarction (NSTEMI). Patients were 75 years or older from 1 of 3 Swedish hospitals. Frailty was defined using the Canadian Study of Health and Aging Clinical Frailty Scale, which groups patients into 1 of 7 categories of increasing dependence on others due to comorbidity, disability, or cognitive impairment.[17] This frailty scale does not require physical performance measures, only clinical judgment. Of 307 patients, 49% were considered frail (score, 5–7). Using logistic regression, frailty was independently associated with the primary composite outcome (death, reinfarction, revascularization due to ischemia, hospitalization, major bleeding, stroke/transient ischemic attack, need for dialysis up to 1 month after inclusion) (odds ratio, 2.2), in-hospital mortality (odds ratio, 4.7), and 1-month mortality (odds ratio, 4.7). Frail patients were less likely to undergo cardiac catheterization or intensive care unit admission.

Conclusion: The traditional assessment of frailty using hand-grip strength, gait speed, and other measures is often cumbersome in the clinical setting. The authors' primary contribution may therefore have been their use of a simple predictive scale that relies only on clinical judgment to stratify patients into 1 of 7 risk categories. To promote the common use and integration of frailty indices with popular risk models in patients with NSTEMI and unstable angina such as the Thrombolysis In Myocardial Infarction risk score, frailty assessment tools must have high interrater reliability and must be easy to use.[18]

Addition of Frailty and Disability to Cardiac Surgery Risk Scores Identifies Elderly Patients at High Risk of Mortality or Major Morbidity

Summary: Cardiac surgical risk scores in common use such as the EuroSCORE are known to perform less well in the elderly, in part because they do not account for important phenotypic characteristics including frailty and disability that correlate with greater adverse outcomes. The authors therefore tested the discriminative utility of 4 frailty scales (5-meter gait speed, Cardiovascular Health Study [CHS] scale, modified CHS scale, MacArthur Study of Successful Aging scale) and 3 disability scales (Katz Activities of Daily Living [ADL], Katz IADL, Nagi scale) when added to 5 cardiac surgery risk scores (Parsonnet score, Society of Thoracic Surgeons (STS)-predicted mortality and morbidity score, STS predicted mortality score, logistic EuroSCORE, age creatinine ejection fraction score) for postoperative mortality or major morbidity. Of 152 prospectively enrolled patients undergoing bypass and/or valve surgery, mean age was 75.9 years. Depending on the scale used, 20% to 46% were frail and 5% to 76% had at least 1 disability. The scales most predictive of adverse outcomes were 5-meter gait speed (odds ratio, 2.6) and greater than 3 impairments on the Nagi disability scale (odds ratio, 3). When these were added to Parsonnet and STS Mortality and Morbidity scores, model discrimination improved with the area under the curve increasing modestly from 0.68 to 0.72 to 0.73 to 0.76.

Conclusion: This study demonstrates the potential utility of combining markers of frailty and disability with traditional surgical risk scores. For years, these more formal markers of functional status have been largely ignored not just by the surgical community but also by practicing cardiologists when performing their preoperative assessments. Additional geriatric syndromes including hearing and vision loss, a propensity to fall, and cognitive impairment may also provide prognostic information before surgery but have not been formally evaluated with the same rigor as frailty.[19]

Procedural Interventions in the Elderly

Cardiovascular disease is the leading cause of morbidity and mortality in older persons. Accordingly, a significant proportion of the elderly receive invasive cardiovascular interventions such percutaneous coronary interventions (PCIs) or implantation of a cardioverter-defibrillator (ICD). A quarter of PCIs are performed in patients above the age of 75 years, and almost half of the ICD recipients are above the age of 70 years.[20–22] Yet, despite the widespread application of these interventions, we lack a detailed understanding regarding their precise effectiveness as well as anticipated harm in older persons, especially the "oldest old" (persons above the age of 85 years). This group has been largely excluded from clinical trials and has often been passed over for treatment even in the real world, as perceived harms have affected treatment decisions to a greater degree than anticipated absolute benefits.[23]

In the following section, we include a variety of studies looking at procedural interventions in the elderly, including transcatheter aortic valve replacement, implantation of a cardioverter-defibrillator, and abdominal aneurysm repair.

Clinical Effectiveness of Implantable Cardioverter-Defibrillators Among Medicare Beneficiaries With Heart Failure

Summary: The clinical effectiveness of implantable cardioverter-defibrillators (ICDs) in older patients with heart failure has not been established. The authors identified 4685 hospitalized patients with heart failure who were aged 65 years or older and were eligible for an ICD, had left ventricular ejection fraction of $\leq35\%$, and were discharged alive from hospitals participating in the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure (OPTIMIZE-HF) and the Get With The Guidelines–Heart Failure (GWTG-HF) quality-improvement programs during the period January 1, 2003, through December 31, 2006. These patients were matched to Medicare claims to examine long-term outcomes. The main outcome measure was all-cause mortality over 3 years. Mean age was 75.2 years, 60% of the patients were women, mean ejection fraction was 25%, and 376 (8.0%) patients received an ICD before discharge. Mortality was significantly lower among patients who received an ICD before discharge compared with those who did not (19.8% versus 27.6% at 1 year, 30.9% versus 41.9% at 2 years, and 38.1% versus 52.3% at 3 years; $P<0.001$ for all comparisons). The inverse probability-weighted adjusted hazard of mortality at 3 years for patients receiving an ICD at discharge was 0.71.

Conclusion: ICD placement before discharge was associated with a mortality benefit among qualifying older persons hospitalized with heart failure. The reduced mortality rate in the group receiving an ICD was comparable to randomized, controlled trials involving younger patients.[24,25] However, it is possible that the small number of patients receiving an ICD during the initial hospitalization were less acutely ill in ways not captured fully by risk adjustment and therefore would be expected to have better long-term outcomes.[26]

Determinants of Cardiac Catheterization Use in Older Medicare Patients With Acute Myocardial Infarction

Summary: Data have consistently demonstrated suboptimal patient selection for cardiac catheterization in acute myocardial infarction (AMI). Using data of Medicare fee-for-service beneficiaries hospitalized with AMI between 1998 and 2001, the authors developed multivariate models to determine the relative influence of anticipated benefit (baseline cardiovascular risk), anticipated harm (bleeding risk, comorbidities), and patient demographic factors (age, sex, race, regional invasive intensity) in predicting cardiac catheterization within 60 days of admission. Analyses were stratified by appropriateness criteria using American College of Cardiology/American Heart Association guidelines. Class I or II recommendations were considered appropriate, and class III recommendations were considered inappropriate. Determinants of a reduced likelihood of cardiac catheterization among the 42 241 AMI patients with appropriate indications included older age (likelihood $\chi^2=1309.5$), higher bleeding risk score (likelihood $\chi^2=471.2$), more comorbidities (likelihood $\chi^2=276.6$), female sex (likelihood $\chi^2=162.9$), hospitalization in low-intensity (likelihood $\chi^2=67.9$) or intermediate-intensity invasive regions (likelihood $\chi^2=22.4$), and baseline cardiovascular risk (likelihood $\chi^2=6.4$) (all $P\leq0.01$). Among 2398 AMI patients with inappropriate indications, significant determinants of greater procedure likelihood included younger age, male sex, lower bleeding risk score, and fewer comorbidities.

Conclusion: The authors have illustrated that the anticipated harm from cardiac catheterization often takes precedence over the potential procedural benefits in typical clinical decision-making for high-risk patients. Because practice guidelines are often developed from data drawn from randomized trials that usually enroll low-risk patients, it is uncertain as to how these results generalize to patient mix in the real world. In the absence of further studies among high-risk patients, recommendations to practitioners should highlight potential procedural benefits, not just harms, in high-risk patients.[23]

Operative and Middle-Term Results of Cardiac Surgery in Nonagenarians: A Bridge Toward Routine Practice

Summary: Nonagenarians are among the fastest-growing sectors of the population, yet cardiac surgical outcomes in this group are relatively unknown. The authors therefore analyzed the operative and 5-year follow-up results of 127 patients aged 90 years or above who underwent cardiac surgery from 1998 to 2008. Mean age was 92 years (range, 90–103). Operative mortality was 13% as opposed to the expected 21% predicted by the logistic EuroSCORE. Higher overall mortality was seen among patients having nonelective surgery; 43% had postoperative complications such as surgical revision for bleeding, postoperative respiratory insufficiency, acute renal failure, neurological complications, and sternal wound infection. Mean hospitalization time of those surviving the initial surgery was 29.2 days (range, 16–68 days), which included postoperative cardiac rehabilitation. Five-year mortality among patients surviving the initial operation was 41%.

Conclusion: Although the authors emphasize the potential benefits of cardiac surgery among appropriately selected nonagenarians, both postoperative complications and mortality within 5 years of surgery were extremely common. In addition, average postoperative hospitalization time even among survivors was approximately 1 month. Although not directly reported, time spent in skilled nursing facilities probably was substantial. To support patient-centered decision-making, information on expected postoperative complications and hospital stay should become a standard part of preoperative patient education and informed consent.[27]

Aortic Valve Replacement in the Elderly: Determinants of Late Outcome

Summary: Few data exist on long-term outcomes of elderly patients after aortic valve replacement. The authors retrospectively evaluated 2890 consecutive patients >70 years of age who underwent aortic valve replacement between January 1993 and December 2007 and stratified them by preoperative and intraoperative variables. They used the Olmsted County, Minnesota, general population database for comparative survival analysis. Observed 5-, 10-, and 15-year late postoperative survival rates were lower than those of an age- and sex-matched healthy population (68%, 34%, and 8% versus 70%, 42% and 20%, respectively). Independent predictors of late death included older age, renal failure, diabetes mellitus, stroke, myocardial infarction, immunosuppression, prior coronary artery bypass grafting, implanted pacemaker, lower ejection fraction, hypertension, and New York Heart Association class III or IV. After

stratification by an age-comorbidity risk score developed on the basis of a multivariate Cox regression model, 10-year survival for the lowest-risk group (n=946) was similar to expected survival (55% versus 55%), but, for the highest-risk group (n=564), survival was significantly lower than expected (9% versus 26%). For 229 pairs of propensity-matched patients with mechanical or biological prostheses, survival was not significantly different (67%, 40%, and 19% versus 71%, 45%, and 7% at 5, 10, and 15 years, respectively; $P<0.81$). Structural deterioration of bioprostheses occurred in only 64 patients (2.4%).

Conclusion: Choice of optimal surgical strategy for aortic valve replacement in the elderly has tended to favor bioprosthetic compared with mechanical valves because of increased risk of major hemorrhagic or embolic events associated with the latter. The low rates of structural deterioration with aortic bioprosthesis and comparable survival associated with either valve category are reassuring findings for continued use of bioprosthetic valves among older patients.[28]

Influence of Age on Perioperative Complications Among Patients Undergoing Implantable Cardioverter-Defibrillators for Primary Prevention in the United States

Summary: The authors examined data on periprocedural complications associated with implantable cardioverter-defibrillator (ICD) implantation for primary prevention among older persons in the United States. Using the National Cardiovascular Data Registry, the authors identified 150 264 patients who received an ICD from January 2006 to December 2008. The primary end point was any adverse event or death during hospitalization. Secondary end points included major adverse events, minor adverse events, and length of stay. Of 150 264 patients, 61% (n=91 863) were 65 years and older. A higher proportion of patients ≥65 years of age had diabetes, congestive heart failure, atrial fibrillation, renal disease, and coronary artery disease. The rate of adverse events or death was 2.8%, 3.1%, 3.5%, 3.9%, 4.5%, and 4.5%, respectively in patients under 65 years, 65- to 69-year-olds, 70- to 74-year-olds,75- to 79-year-olds, 80- to 84-year-olds, and patients 85 years and older. After adjustment for clinical covariates, multivariate analysis found a significantly increased odds ($P≤0.05$) of any adverse event or death among 75- to 79-year-olds (odds ratio [OR], 1.14), 80- to 84-year-olds (OR, 1.22), and patients 85 years and older (OR, 1.15), compared with patients under 65 years of age.

Conclusion: Age remains a prognostic factor for periprocedural complications related to ICD placement. Patients should be made aware of how their individual risk changes due to age and other prognostic factors before device placement. Implementation of point-of-care tools that accurately describe procedural risks based on individual patient characteristics should be a priority to promote evidence-based decision-making.[29]

Survival After Open Versus Endovascular Thoracic Aortic Aneurysm Repair in an Observational Study of the Medicare Population

Summary: The authors of the study compared the short- and long-term survival of patients with descending thoracic aortic aneurysms (TAAs) after open and endovascular repair (TEVAR). By using a combination of procedural and diagnostic *International Classification of Disease, 9th Revision* codes, the authors analyzed patients who underwent repair for intact as well as ruptured TAAs using Medicare claims from 1998 to 2007. They examined perioperative mortality (death occurring before hospital discharge or within 30 days) and 5-year survival across repair type (open repair or TEVAR) in crude, adjusted (for age, sex, race, procedure year, and Charlson comorbidity score), and propensity-matched co-

horts. Overall, 12 573 Medicare patients underwent open repair and 2732 patients underwent TEVAR. Perioperative mortality was lower in patients undergoing TEVAR compared with open repair for both intact (6.1% versus 7.1%; $P=0.07$) and ruptured (28% versus 46%; $P<0.0001$) TAA. However, patients with intact TAA who underwent TEVAR had significantly worse survival than open patients at 1 year (87% for open, 82% for TEVAR; $P=0.001$) and 5 years (72% for open; 62% for TEVAR; $P=0.001$). Patients in adjusted and propensity-matched cohorts had similarly worse 5-year outcome with TEVAR.

Conclusion: This study demonstrates using real-world data that the mortality benefit conferred by endovascular repair compared with open surgical repair for TAA is limited to the perioperative period. Though a higher-risk group of patients underwent endovascular repair, their worse long-term outcomes despite adjustment for demographics, comorbidity, and rupture status calls into question the relative efficacy of TEVAR, especially as more relatively healthy patients have elected to have endovascular treatment versus traditional operative repair in recent years.[30–32]

Incidence and Predictors of Early and Late Mortality After Transcatheter Aortic Valve Implantation in 663 Patients With Severe Aortic Stenosis

Summary: There is a lack of information on the incidence and predictors of both early mortality at 30 days and late mortality between 30 days and 1 year after transcatheter aortic valve implantation (TAVI) with the self-expanding CoreValve Revalving prosthesis. The authors studied a total of 663 consecutive patients (mean age, 81 years) who underwent TAVI with the third-generation 18-F CoreValve device in 14 centers. Procedural success and intraprocedural mortality were 98% and 0.9%, respectively. The cumulative incidences of mortality were 5.4% at 30 days, 12.2% at 6 months, and 15.0% at 1 year. Clinical and hemodynamic benefits observed acutely after TAVI were sustained at 1 year. Paravalvular leakages were trace to mild in the majority of cases. Conversion to open heart surgery, cardiac tamponade, major access site complications, left ventricular ejection fraction <40%, prior balloon valvuloplasty, and diabetes mellitus were independent predictors of mortality at 30 days, whereas prior stroke, postprocedural paravalvular leak ≥2+ prior acute pulmonary edema, and chronic kidney disease were independent predictors of mortality between 30 days and 1 year. The discriminative ability of the logistic EuroSCORE for predicting the risk of 30-day and 1-year mortality was weak (c-statistic, 0.55 for both).

Conclusion: TAVI has emerged as a promising treatment option for nonsurgical high-risk patients with symptomatic severe aortic stenosis in the recent years. The data from this study showed that while early mortality was mainly affected by procedural complications, late mortality was influenced primarily by comorbidities. Importantly, the logistic Euro-SCORE showed a weak discriminative ability in predicting 30-day and 1-year mortality, highlighting the need for novel TAVI-specific scores, such as the recently proposed Karnofsky index used in the post-TAVI setting.[33,34]

Clopidogrel Use and Early Outcomes Among Older Patients Receiving a Drug-Eluting Coronary Artery Stent

Summary: Although clopidogrel administration after drug-eluting stent (DES) implantation is essential for the prevention of early in-stent thrombosis, its use among older DES recipients has not been widely studied. The authors sought to identify characteristics associated with failure to fill a clopidogrel prescription and to examine the relationship between filling the prescription and hospitalization for acute myocardial infarction (AMI) or death. Administrative data of 15 996 Medicare Part D enrollees who received a DES during

2006 to 2007 were analyzed. The authors modeled the adjusted probability and odds of filling a prescription for clopidogrel within 7 and 90 days of discharge and its association with AMI hospitalization or death. Of the study sample, 19.7% did not fill a clopidogrel prescription within 7 days of discharge. This percentage fell to 13.3% by day 90. The adjusted probability of filling a clopidogrel prescription within 7 or 90 days of discharge was lower for patients with dementia (20.2% less likely), depression (10.7% less likely), age >84 years compared with age 65 to 69 years (10.6% less likely), black race (6.6% less likely), intermediate levels of medication cost share (5.2% less likely), and female sex (3.3% less likely). Prescription filling was higher for patients initially hospitalized for an AMI (12.5% more likely). Failure to fill a clopidogrel prescription within 7 days of discharge was associated with a higher risk of death during days 8 to 90 (adjusted odds ratio, 2.44) but was not associated with an increased risk of hospitalization for AMI.

Conclusion: Despite class 1A recommendation of prolonged dual antiplatelet therapy after DES placement, it is concerning that 1 in 5 patients failed to fill a prescription for clopidogrel soon after DES implantation and that 1 in 7 still were not taking the medication 3 months after the procedure. Given their increased likelihood of nonadherence, patients with advanced age, dementia, and depression may require closer follow-up and additional assistance after the procedure.[35]

Cost-Effectiveness of Transcatheter Aortic Valve Replacement Compared With Standard Care Among Inoperable Patients With Severe Aortic Stenosis: Results From the Placement of Aortic Transcatheter Valves (PARTNER) Trial (Cohort B)

Summary: In patients with severe aortic stenosis who cannot have surgery, transcatheter aortic valve replacement (TAVR) has been shown to improve survival and quality of life compared with standard therapy, but the costs and cost-effectiveness of this strategy are yet unknown. The PARTNER trial randomized patients with symptomatic, severe aortic stenosis who were not candidates for surgery to TAVR (n=179) or standard therapy (n=179). Empirical data regarding survival, quality of life, medical resource use, and hospital costs were collected during the trial and used to project life expectancy, quality-adjusted life expectancy, and lifetime medical care costs to estimate the incremental cost-effectiveness of TAVR from a US perspective. For patients treated with TAVR, mean costs for the initial procedure and hospitalization were $42 806 and $78 542, respectively. Follow-up costs through 12 months were lower with TAVR relative to medical management ($29 289 versus $53 621) because of reduced hospitalization rates, but cumulative 1-year costs remained higher ($106 076 versus $53 621). The authors projected that over a patient's lifetime, TAVR would increase discounted life expectancy by 1.6 years (1.3 quality-adjusted life-years), at an incremental cost of $79 837. The incremental cost-effectiveness ratio for TAVR was thus estimated at $50 200 per year of life gained or $61 889 per quality-adjusted life-year gained.

Conclusion: As TAVR is being increasingly adopted as a treatment modality for elderly patients with severe symptomatic aortic stenosis not eligible for open surgery, assessment of its cost-effectiveness in today's era of constrained economy is important. Results from the PARTNER trial demonstrating the cost-effectiveness of this procedure indicate that TAVR will be a promising therapeutic modality as postprocedural complications decline, prosthetic valves improve in performance, and patient selection improves. However, the results were sensitive to multiple assumptions such as estimations of life expectancy and costs beyond the first year of follow-up, mandating careful interpretation of results.[36]

Heart Failure in the Elderly

Heart failure (HF) is the leading cause of hospitalization and rehospitalization among elderly patients. With improved care and survival of patients with acute myocardial infarction, as well as improved HF survival rates, the number of elderly patients with HF is on the rise.[37,38]

Randomized trials are difficult to conduct in older persons, and many recommendations are extrapolated from studies in younger patients. Greater burden of comorbidities, frequent contraindications to HF therapies, and functional and cognitive impairment further complicate disease course and outcomes in the elderly.[2,39]

In addition, treatment preferences may vary with patient age. Many elderly HF patients might favor treatment options that improve their life quality and functional status, even at the cost of greater mortality. Older patients with decompensated HF may elect to stay at home rather than being hospitalized; once hospitalized, they may seek alternative post–acute care options besides discharge to a skilled nursing facility.

The summaries in this section include articles concerning the efficacy of exercise training among patients with HF, outcomes for general HF patients in transplant versus nontransplant hospitals, and the discharge planning process.

Thirty-Day Outcomes in Medicare Patients With Heart Failure at Heart Transplant Centers

Summary: Heart transplant centers are thought to provide the ultimate specialist-directed care for advanced heart failure (HF) patients. It is unclear, however, whether such hospitals provide higher levels of care for their overall population of elderly HF patients, the great majority of whom are not transplant recipients. This study compared 30-day risk-standardized mortality rates (RSMRs) and 30-day risk-standardized readmission rates (RSRRs) for transplant and nontransplant hospitals, using the methodology used by the Centers for Medicare and Medicaid Services for public reporting. Compared with nontransplant hospitals, transplant centers had lower RSMRs (10.6% versus 11.5%, $P<0.001$). However, the RSMRs at transplant centers were similar to those from large bypass surgery–capable teaching hospitals located in the same hospital referral regions (10.6% versus 10.6%, $P=0.96$). Heart transplant centers were comparable with other centers in risk-standardized readmission rates.

Conclusion: For elderly HF patients, heart transplant centers had RSMRs that were overall lower than nontransplant centers but were as good as large surgery-capable hospitals in their same hospital referral region. These findings suggest that the mortality benefit seen at heart transplant centers may stem from more general cardiovascular and surgical resources, as well as direct care delivery by cardiologists and improved adherence to guidelines-driven HF therapy, rather than transplant-specific capabilities and facilities.[39]

Exercise Training in Older Patients With Heart Failure and Preserved Ejection Fraction: A Randomized, Controlled, Single-Blind Trial

Summary: Limited exercise capacity is an important contributor to reduced life quality and is an independent predictor of mortality among heart failure (HF) patients. Whereas many of the HF patients—including the majority of elderly HF patients—have HF with preserved systolic function (HFPSF), the impact of exercise training on patients with HFPSF is unknown. In a small, randomized, controlled, single-blind trial, the authors tested the effects of a 16-week aerobic exercise training program in patients with isolated HFPSF. Control patients received biweekly follow-up phone calls. Forty-six of the 53 patients in the study completed the follow-up testing (24 from the exercise group and 22 control subjects). Exercise training improved peak oxygen uptake (13.8±2.5 to 16.1±2.6 mL/kg per minute versus 12.8±2.6 to 12.5±3.4 mL/kg per minute, $P=0.0002$) and 6-minute walk distance ($P=0.002$). There was no

evidence of cardiac biomarker or echocardiographic improvement after completion of 16-week exercise training program. Even though physical quality of life (QOL) score was improved ($P=0.03$), the trend for improvement in total QOL did not reach statistical significance ($P=0.11$).

Conclusion: Nearly half of HF patients present with HFPSF, yet we lack effective treatments for these patients. This is the first study to evaluate the impact of exercise training in patients with HFPSF. Although this study met its primary surrogate end point of improve peak oxygen uptake, overall QOL was not improved. Therefore, at this time, it is not appropriate to promote exercise programs as improving important patient-centered outcomes without evidence of further benefits.[40]

Discharge to a Skilled Nursing Facility and Subsequent Clinical Outcomes Among Older Patients Hospitalized for Heart Failure

Summary: Heart failure (HF) is the leading cause of hospitalization and readmission among older patients. This study prominently examines the association between discharge destination and outcome. The authors analyzed 15 459 Medicare beneficiaries ≥65 years of age who were discharged alive to a skilled nursing facility (SNF) or home after a 3-day or longer hospitalization for HF in 2005 and 2006. All patients had records within the Get With The Guidelines–Heart Failure Registry; 24.1% of patients were discharged to an SNF, 22.3% to home with home health services, and 53.6% to home with self-care. Patients discharged to an SNF had a median age of 80 years. More than half were women, nearly half had ischemic heart disease, and their median length of hospital stay before discharge was 5 days. Unadjusted absolute event rates at 30 days (14.4% versus 4.1% for death and 27.0% versus 23.5% for readmission) and 1 year (53.5% versus 29.1% for death and76.1% versus 72.2% for readmission) were markedly higher for patients discharged to an SNF compared with patients discharged elsewhere ($P<0.0001$ for all). Discharge to an SNF remained associated with increased death (hazard ratio, 1.76) and readmission (hazard ratio, 1.08) after adjustment for measured patient characteristics.

Conclusion: Each year, HF accounts for more than 1 million hospitalizations; of these, 1 of 5 is discharged to an SNF. Patients discharged to an SNF are at increased risk for adverse events, and approximately 50% die within 1 year after hospital discharge. Given this strikingly high rate of predicted mortality, advanced care planning and consideration for palliative care referral should be strongly considered for all HF patients discharged to an SNF.[41]

Impact of Progression of Diastolic Dysfunction on Mortality in Patients With Normal Ejection Fraction

Summary: The aim of this study was to evaluate the impact of progression in diastolic dysfunction on mortality. The study cohort consisted of 1065 outpatients who had preserved left ventricular ejection fraction (LVEF) on a baseline clinically indicated echocardiogram and who had a second clinically indicated echocardiogram 6 to 24 months later. Of these, 770 (73%) patients were noted to have abnormal baseline diastolic dysfunction. On follow-up testing (mean, 1.1 ± 0.4 years), 88 (8.3%) patients had a decrease in LVEF to <55% and were more likely to have advanced diastolic dysfunction ($P=0.0002$). After further follow-up of 1.6 ± 0.8 years, 142 patients (13%) had died. Of these 142 patients, 122 had worsening of diastolic function. On multivariate analysis, a decrease in LVEF to <55% and any worsening of diastolic function on follow-up echocardiography were independently associated with increased risk of mortality (respective hazard ratios, 1.78 with $P=0.02$ and 1.78 with $P=0.003$).

Conclusion: Worsening of diastolic function independently predicts mortality to a similar degree as worsening LV systolic function to <55%. This result is particularly pertinent to older patients with HF, the majority of whom have HF with preserved ejection fraction in part due to diastolic relaxation abnormalities. Unfortunately, treatment options to improve diastolic dysfunction are limited at the current time.[42]

Efficacy and Cost of an Exercise Program for Functionally Impaired Older Patients With Heart Failure: A Randomized, Controlled Trial

Summary: Many heart failure (HF) patients have functional impairment, which reduces their life quality. This randomized, controlled trial tested whether a tailored exercise training program, comprising a mixture of aerobic exercise and resistance-training with gradual increments over time, could improve exercise capacity and life quality among elderly HF patients with left ventricular systolic dysfunction and New York Heart Association class II or III status. Exercise training was conducted at an exercise class by a physiotherapist for 8 weeks and was followed by 16 weeks of home exercise. Forty-one of the 53 patients randomized to the exercise program attended ≥80% of the sessions offered during the first 8 weeks. Exercise training did not improve 6-minute walk distance at 8 weeks or at 24 weeks (−16.9 m; 95% confidence interval, −41.8 to 7.9 m; $P=0.18$, and −5.3 m; 95% confidence interval, −32.6 to 22.0 m; $P=0.70$, respectively). Similarly, patient quality of life and caregiver strain did not improve at 24-week follow-up. The exercise intervention was not cost-saving.

Conclusion: Training programs have been shown to improve exercise capacity and quality of life in younger HF patients. However, findings of this study, in line with other recent studies, do not confirm similar benefits in the elderly.[43,44] In this case, exercise did not improve either 6-minute walk distance or the secondary end points of patient quality of life and caregiver strain. Given its lack of proven efficacy and potential association with harm including injury and cardiovascular decompensation among the functionally impaired, exercise training in elderly HF patients cannot be universally recommended and should be used only with caution.[45]

Anticoagulation in the Elderly

The topic of anticoagulation in the elderly has been a source of polarized opinions. On the one hand, elderly patients have the greatest absolute risk of adverse outcomes from venous thrombosis and cardioembolism. On the other hand, absolute risks of bleeding also increase with age and frequently associated comorbidities and other pharmacotherapies. The recent advent of newer oral anticoagulant agents[46] that have been shown to confer efficacy similar to warfarin with less bleeding in properly selected candidates may promote further uptake of anticoagulation. Yet, the risks remain real,[47] and proper patient selection will remain critical as we move toward greater use of oral agents.

Cognitive Function and Anticoagulation Control in Patients With Atrial Fibrillation

Summary: Atrial fibrillation (AF) is an important comorbidity in the aging population, in whom cognitive dysfunction is common and may impair appropriate anticoagulation, leading to excess vascular events and bleeding. Using the data from the Atrial Fibrillation Clopidogrel Trial With Irbesartan for Prevention of Vascular Events (ACTIVE-W) trial, the authors tested the association between cognitive dysfunction and appropriate anticoagulation, as well as ensuing outcomes. Cognitive function was assessed by the Mini-Mental State Examination (MMSE), with values <26 being suggestive of cognitive impairment. Appropriateness of anticoagulation was assessed using the time in therapeutic range (TTR), which reflects the time duration in which the international normalized ratio is kept between 2.0 and 3.0. Among 2510 participants receiving oral anticoagulation who had complete data, 365 patients had MMSE scores <26. Over a follow-up period of 1.3 years, the median TTR

was 65% in the overall cohort. MMSE score <26 was an independent predictor of lower TTR. Moreover, vascular events and bleeding were both less frequently seen among patients with MMSE scores ≥26 (hazard ratio, 0.46; 95% confidence interval, 0.27–0.78; $P=0.002$ and hazard ratio, 0.56; 95% confidence interval, 0.37–0.85; $P=0.04$, correspondingly). The MMSE score was not a predictor of vascular events or bleeding after adjustment for TTR.

Conclusion: More elderly AF patients in the real-world setting have cognitive impairment relative to randomized trial populations. In this study, cognitive impairment was associated with worse bleeding and stroke outcomes among elderly AF patients, in part due to suboptimal TTR. Therefore, when anticoagulation is initiated in patients with cognitive dysfunction, extra care, such as enrollment in anticoagulation clinics, involvement of caregivers, and simplified medication instructions, may be helpful. If safety remains a concern, a decision not-to-treat may be appropriate.[48]

Use of Antithrombotic Medications Among Elderly Ischemic Stroke Patients

Summary: The use of antithrombotic medications after ischemic stroke is recommended for deep vein thrombosis (DVT) prophylaxis and secondary stroke prevention. The authors assessed the rate of receipt of these therapies among eligible ischemic stroke patients with age >65 years and then determined the effects of age and other patient characteristics on treatment. Study participants were part of the Medicare Health Care Quality Improvement Program's National Stroke Project. The authors identified 31 554 Medicare fee-for-service beneficiaries discharged with a primary diagnosis of ischemic stroke from 2 periods of data collection (1998–1999 and 2000–2001). Receipt of in-hospital pharmacological DVT prophylaxis, antiplatelet medication, anticoagulants for atrial fibrillation, and antithrombotic medications at discharge were assessed in eligible patients who were stratified by age. Among the patients studied, 14.9% of those eligible received pharmacological DVT prophylaxis, 83.9% received antiplatelet drugs, and 82.8% received anticoagulants for atrial fibrillation; 74.2% of patients were discharged on an antithrombotic medication. Rates of appropriate treatment decreased with age and were lowest for patients aged 85 years or older. Admission from a skilled nursing facility and functional dependence were associated with lower treatment rates.

Conclusion: This study demonstrated that advanced patient age may influence clinical decision-making regarding the use of antithrombotics among patients with stroke. This finding mirrors previous studies showing that older and higher-risk patients are less likely to get evidence-based therapy after myocardial infarction. The source of this undertreatment may reflect excessive concern among providers about bleeding complications, insufficient use of caregivers when trying to implement a postdischarge medication plan, patient preferences against antithrombotics, or other reasons. Hospitals should introduce additional measures to ensure that older and higher-risk patients can safely receive guideline-based therapy.[49]

Bleeding Risk in Very Old Patients on Vitamin K Antagonist Treatment: Results of a Prospective Collaborative Study on Elderly Patients Followed by Italian Centres for Anticoagulation

Summary: Vitamin K antagonist (VKA) therapy is indicated for the prevention of venous thromboembolism (VTE) and stroke in atrial fibrillation (AF). Risk of bleeding is a major concern for VKA prescription, especially in very old patients who have multiple comorbidities. To evaluate the quality of anticoagulation and the incidence of bleeding in the elderly, the authors performed a large, multicenter, prospective, observational study enrolling 4093 patients over the age of 80 years who were naive to VKA for thromboprophylaxis of AF or after VTE. Patients' demographic and clinical data

were collected, and the quality of anticoagulation and the incidence of bleeding were recorded. Patient characteristics were remarkable for a creatinine clearance <50 mL/min in 60.6% patients. Rates of major bleeding and fatal bleeding were 1.87 per 100 patient-years and 0.27 per 100 patient-years, respectively. The rate of bleeding was higher in men compared with women (relative risk, 1.4; $P=0.002$) and among patients >85 years of age compared with younger patients (relative risk, 1.3; $P=0.048$). Time in therapeutic range was 62% (interquartile range, 49% to 75%). History of bleeding, active cancer, and history of falls were independently associated with bleeding risk.

Conclusion: The low bleeding rates in the setting of optimal quality of anticoagulation observed in this study support aggressive anticoagulant therapy with VKA in geriatric patients with VTE or AF. These findings are particularly relevant for the elderly, who have been shown to receive suboptimal anticoagulation due to excessive fears regarding bleeding. Interestingly, more than half of the entire cohort showed a creatinine clearance of <50 mL/min, thereby raising a concern for careful utilization of renally excreted newer anticoagulant agents such as dabigatran.[50]

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