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Percutaneous coronary intervention in the elderly: a growing need for a growing population

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Persons aged 80 and above are the fastest growing age group in the United States population, having increased 50% since 1990 and predicted to grow another 25% by 2020. As this aging population grows, heart disease remains the leading cause of death, accounting for 30% of deaths in the 75-84 age group and 37% for those aged greater than 85 years. Similar trends are apparent throughout much of the rest of the world. As the elderly population increases and technology advances, more and more elderly patients undergo coronary angiography and percutaneous coronary intervention (PCI). In a large series of patients from Northern New England in the US, 4% of all PCI procedures were performed in patients aged 80 or greater between 1989 and 1993, increasing to 8%-9% of all PCI procedures in 1998-2003. In an even larger meta-analysis of combined studies, the incidence of PCI in patients aged 75 or older increased between 1990 and 1999 from 12% to 22%.

The outcomes following any procedure in the elderly are known to be worse than in younger patients and this has been documented in many studies of PCI in the elderly. It is, however, difficult to evaluate the results of PCI compared to other treatment approaches. The elderly are mostly excluded from randomized trial studies. Registry studies include the elderly but represent small series or larger number of patients either from experienced high volume centers or from multiple centers with varying outcomes. All clearly involve considerable selection bias in deciding on an interventional approach for these patients. Furthermore, since the elderly have higher mortality rates and shorter life expectancy, comparisons of different treatment options are difficult and it may be less important to provide improvement in mortality than to improve quality of life in these patients. Unfortunately, the latter is rarely studied.

Clinical characteristics of the elderly PCI population

The elderly are not only older but are generally sicker with significantly more co-morbidities. Studies of PCIs in patients aged 75-80 have invariably shown, compared to younger patients having PCI, a higher incidence of females, diabetes, hypertension, history of congestive heart failure, renal failure, peripheral vascular disease, pulmonary disease, prior coronary artery bypass graft (CABG) surgery, prior myocardial infarction (MI), unstable angina, acute myocardial infarction (AMI), and cerebrovascular disease. Multivessel disease is more likely, as is left main disease and complex type B2 and C lesions. PCI procedures are more frequently urgent or emergent. There appears to be little change in these patient characteristics in various series reported over different time periods.

All of these features have been associated with worse PCI outcomes in the overall population. Therefore, adverse outcomes in the elderly would be expected to be higher. Since the proportion of elderly patients with coronary artery disease having angiography and revascularization is smaller than in younger age groups, there is clearly a selection process with those selected for PCI likely better candidates than those who are not. It becomes particularly important in these elderly patients to make appropriate decisions as to the risks and benefits to be anticipated from intervention.

Inhospital outcomes of PCI in the elderly

In early percutaneous transluminal coronary angioplasty (PTCA) experience, outcomes were significantly worse in older patients. In the 1985-1986 NHLBI registry, including 486 patients aged 65 and older, older patients had similar angiographic success but significantly worse inhospital mortality (3.3% for age 75 or greater, 3.0% for ages 65-74, and 0.2% for age less than 65 years). In 474 patients aged 75 and older having PTCA in 1991-1992, reported from a single high volume center, inhospital mortality was 2.1% for age 75 or greater, 1.1% for ages 65-74, and 0.5% for age less than 65 years. Mortality and major adverse cardiac events...
(MACE), including MI, need for transfusion, and vascular repair, were independently predicted by age. Despite this, there was no difference in procedural success or need for urgent CABG.\(^8\)

In the US Medicare experience from 1987-1990\(^\text{a}\) of all 225,916 patients aged 65 and older having PTCA, 30 day mortality after PTCA increased from 2.1% for ages 65-69 to 7.8% for age 80 and older.\(^9\) In a large series of 12,172 patients having PTCA at large volume hospital centers in Northern New England in the US, 507 patients (4%) were aged 80 and greater. Inhospital mortality significantly increased by decade from 0.4% for ages less than 60 to 3.2% for ages 80 and older. After adjustment for other variables affecting outcome, age greater than 70 predicted a 5-fold increase in hospital mortality. In this series, there was no change in lesion success rate, occurrence of non-fatal MI, or emergent CABG with increasing patient age.\(^2\)

The advent of coronary stenting has considerably improved PCI outcome and lessened the need for urgent CABG in general. Whether this benefit has extended to the elderly is unclear. Peterson et al\(^6\) combined six large PTCA registries from 1991-1999, including more than 48,000 patients. Since this included transition years for use of stents, stenting rate varied from 35% to 58%. Overall, inhospital mortality remained 3.0%, (ranging from 1.5%-5.2% in the different databases), increasing from 1.5% for age less than 65 to 10% at age 90 or greater, with a marked increase apparent at ages greater than 85 years. There was, however, a significant decrease in mortality over time for ages 75 or greater, decreasing from 2.7% in 1991 to 1.2% in 1997, probably as a result of newer technologies, including stents. As expected, mortality was predicted best by emergency procedure, PCI for AMI and cardiogenic shock, and to a lesser extent by left ventricular dysfunction and renal failure. Other adverse inhospital outcomes were low (Q wave MI 0.9%, emergency CABG 1.2%, cerebrovascular accident (CVA) 0.4%, and renal failure 0.8%).

The most recent data from the NHLBI Dynamic Registry\(^5\) included 4,620 PCI patients from 1997-1999 with stents used in 73% and IIb/IIIa platelet inhibitors in 26%-29%. Inhospital mortality remained high at 2.2% for ages 65-79 and 4.6% for ages 80 and older, both significantly increased from ages less than 65 (0.6%). 25% of those aged 80 and greater were treated for AMI and 2% had cardiogenic shock. Use of emergent CABG increased minimally and insignificantly from 1.1% to 1.9% with increasing age. After adjustment for co-morbidities, patients aged 80 and older had a 3-fold increase in risk of hospital death or MI. Similar outcomes were seen in the ACC/NCDR Registry data for 8,828 PCI procedures in octogenarians between 1998 and 2000, with 75% of the patients receiving stents. Procedural success was 93% but inhospital mortality remained high at 3.8%. Recent MI was a very significant predictor of outcomes with mortality of 13.8% if present and only 1.4% if not. Other adverse outcomes were low (Q wave MI 0.5%, CVA 0.5%, renal failure 2.2%, and vascular complications 3.7%).\(^10\)

In a more recent analysis from the Northern New England group, of 60,721 patients between 1994 and 2003, 8% were aged 80 or greater. 65% of the elderly patients received stents and 28% received IIb/IIIa platelet inhibitors. 12% of those patients aged 80 and greater had an emergent procedure. Inhospital mortality occurred in 2.9% of those aged 80 and older, 11% if the procedure was emergent and only 1.9% if non-emergent. After adjustment for co-morbidities, this mortality remained significantly increased compared to patients less than age 60. Non-fatal MI also increased in those aged greater than 70, as did CVA and vascular complications. Clinical success was slightly decreased in the very elderly but was high (91.7%) even in patients aged 80 and greater.\(^3\)

A small study of 26 of the most elderly patients aged 90 and greater, with stents used in 81%, reported success in 92%.\(^11\) Inhospital mortality was very high at 19%, tthough there were no deaths if those with AMI and cardiogenic shock were excluded. Another recent small study of 46 patients aged 80 and greater treated with sirolimus-coated stents reported excellent results. Although 61% had Type B2 and C lesions with 37% involving multi-vessel stenting and 9% left main stenting, there were no inhospital deaths or MACE.\(^12\)

Halon, et al\(^7\) recently reported on consecutive 449 patients aged greater than 70 admitted with acute coronary syndrome. Those aged 80 and greater were generally sicker, more often with AMI and renal failure, and were less likely to have angiography performed than those aged 70-79 (29% vs 44%). However, if angiography was performed, those aged 80 and greater were more likely to have revascularization and revascularization was more likely PCI than CABG compared to patients aged 70-79. Revascularization was actually performed in 23% of both older and younger groups. Selection, therefore, likely resulted in the lower risk more elderly patients having angiography and PCI. Despite this, inpatient mortality was 6% for the very elderly vs 0.8% for those aged 70-79, likely related to the high incidence of AMI (32%) and renal failure (22%) in the very elderly group.

Therefore, despite increasing use of stents and IIb/IIIa platelet inhibitors, inhospital mortality for all patients aged 75-80 remains 3% or higher, significantly more than that for younger age groups. Mortality rate is mark-
edly increased in those patients having emergent procedures and those with AMI and much lower in other elderly patients. However, even when adjusted for clinical factors known to increase risk, age remains a significant predictor of mortality.

Long-term outcomes of PCI in the elderly

Limited data is available concerning longer term outcomes of PCI in the elderly. NHLBI data at one year follow up indicates an increase in mortality by decade from 2.1% for age less than 65 to 4.9% for ages 65-79 and 11% for ages 80 and above. There is also an increased incidence of non-fatal MI (9.4% for age 80 and older compared to 5.8% for age less than 65) which, when risk adjusted, was statistically insignificant. In the series reported by Alfonso, et al., cardiac death at two year follow up was approximately 5% for patients age 65 and greater, slightly but significantly increased compared to age less than 65 with similar rates of restenosis and need for repeat revascularization. The small series of high risk patients treated with a drug-eluting stent reported a one year survival of 91.3% and event-free survival of 89%. Three out of the four deaths in this series were non-cardiac and occurred more than nine months after PCI. In the series of elderly patients presenting with acute coronary syndrome (ACS) reported by Halon, et al., two year survival for all patients regardless of treatment was only 67% for patients aged 80 and greater vs 84% for those aged 70-79. For the 24% of those who were selected for revascularization (78% by PCI), survival was 75% for those aged 80 and greater compared to only 65% for those treated medically, although this was not statistically significant. However, for those oldest patients having revascularization, two year survival was equal to the younger patients aged 70-79, strongly suggesting a benefit for these most elderly patients.

The APPROACH study included all 21,573 patients having cardiac catheterization for ischemic heart disease in Alberta, Canada from 1995-1998. Four year adjusted actuarial survival was reported by patient age groups less than 70, 70-79, and 80 or greater. For all age groups, survival appeared significantly increased for patients having PCI or CABG compared to medical therapy. This was particularly apparent for patients aged 80 and greater (survival 77% with CABG, 72% with PCI, and 60% with medical therapy). Outcomes were similar for patients presenting with stable or unstable angina. The very elderly, therefore, had a greater risk reduction with intervention than younger patients. This series, however, included only those patients who had already been selected for angiography. As a registry study, decision as to treatment strategy was made by individual physicians with selection bias likely affecting which patients were chosen for revascularization. Furthermore, all PCIIs were performed at high volume academic centers in Canada and medical therapy was not standardized. These outcome results, therefore, may not apply in other settings.

Invasive vs medical therapy for elderly patients was evaluated in the randomized TIME study. 301 patients aged 75 and greater with Canadian Cardiac Society (CCS) class II or greater angina on at least two anti-anginal drugs, were randomized to optimal medical therapy or catheterization with revascularization if indicated. Revascularization was actually performed in 72% of the invasive group, 52% by PCI (86% with stents), and 20% by CABG. Patients with AMI, congestive failure, and valvular heart disease were excluded. At six month follow up, mortality was slightly but insignificantly increased in the invasive group (8.5 vs 4.5%) but with half the deaths in the invasive group being in those patients not actually having revascularization. There was a very significant decrease in readmission and revascularization procedures in the invasive group. At one year and four year follow up, the two groups showed no significant difference in death or MI but a continued marked decrease in need for revascularization, a decrease in angina, and increased quality of life in the invasive group.

Nearly all studies of PCI in the elderly have focused on mortality as an outcome. In the very elderly, this may not be the most appropriate measure of success since even the increased mortality rates with PCI seen in these patients may not be higher than that of the general population. Censius data from the United States in 2002 show an overall annual mortality of 7% in all persons aged 80-84, and 15% in those aged 85 and higher. It may therefore be much more important for these patients to consider relief of symptoms and quality of life as the most important outcomes. This has been addressed in very few studies.

Seto, et al reported measures of physical and mental health up to one year after PCI in 295 patients aged 70 or greater with a median age of 74 years who participated in two randomized interventional trials compared to patients in those trials aged less than 70. There was substantial improvement in all measures six and twelve months after PCI in all patients without significant difference between the elderly and the younger patients. As with all randomized trials, it is likely these patients were highly selected, were treated in experience high volume centers, and included very few of the most elderly patients.

In the TIME study as described above, in a relatively small group of patients symptomatic despite medical therapy, quality of life was measured as a primary outcome by standard scores of physical and mental status.
and angina severity. At six month follow up in this study, there was a decrease in angina severity and increased quality of life in those patients randomized to both medical and interventional treatment though more improvement in those with the early invasive approach. However, over this six month initial follow up period, 37% of those initially randomized to medical therapy had revascularization. By one year, both groups continued to have improvement although the early difference between the two groups had disappeared. In the early invasive group, however, there continued to be fewer readmissions for revascularization which had reached 46% in the early medical treatment group. By a median four year follow up, there were very few further revascularization procedures in either group. Both treatment groups continued to have decreased angina severity and increased quality of life compared to baseline with no significant difference between the groups other than requirement for fewer antianginal medications in the early invasive group. However, of those randomized to medical therapy, nearly half, in fact, had revascularization.

Quality of life as a subjective sense of well being was included in the study of patients presenting with ACS reported by Halon, et al. Of interest was that of the surviving patients, those aged 80 and over had a greater improvement in sense of well being than those aged 70-79, whether or not they had received revascularization. This might suggest that very elderly patients benefit from hospital admission and evaluation regardless of whether or not they have intervention. Clinical judgment in decision making as to medical or invasive therapy may, in itself, beneficially affect outcomes.

Available evidence would appear to suggest that elderly patients with coronary disease should be carefully evaluated and treated medically with the decision as to early intervention made after consideration of risk factors. If initially treated medically, they should be followed carefully with angiography if persistent symptoms or instability occurs. Need for revascularization can then be performed depending on angiographic and clinical findings with known increased risk related to age but risk not greater, and likely less, than that with medical therapy alone. The benefits of appropriate earlier revascularization in elderly patients may include earlier relief of symptoms and improvement in quality of life, need for fewer medications, and a decreased risk of later need for revascularization.

PCI versus CABG in the elderly

Hospital mortality for elderly patients undergoing CABG is considerably higher than for younger patients. In a very large series of 8 combined CABG registries for patients aged 75 and older from 1990-1999, hospital mortality ranged from 4.9% to 8.4%, averaging 5.9%. Mortality rates increased approximately 2%/decade to age 85 and increased markedly to 10% after age 85, though with small numbers of these very elderly patients. Other inhospital morbidities were also higher than in younger patients, including CVA 3.5%, renal failure 3.2%, Q wave MI 1.5%, and prolonged ventilatory support 11%. Operative mortality for isolated CABG in octogenarians from the very large Society of Thoracic Surgeons' national cardiac database from 2000-2003 was 6.5%. Such inhospital morbidity and mortality is higher than that reported in most series for PCI. Differences in outcome are, however, very difficult to compare because of selection processes in many cases likely favoring the least sick patients having CABG.

Long-term outcomes are similarly difficult to assess. As previously described in the APPROACH study, four year survival after CABG in octogenarians was 77% vs 60% with medical therapy. Similar outcomes were reported in an earlier study of CABG in octogenarians with one year survival of 81% and three year survival of 71%.

There are no randomized studies comparing CABG with PCI and medical treatment for the very elderly and separate series of these treatment options are difficult to compare because of patient selection involved in treatment. In general, hospital mortality and morbidity is higher with CABG than with PCI and very elderly patients with CABG frequently require prolonged ventilatory support and long hospital and subsequent rehabilitation stays. With appropriate selection, however, longer term outcomes may be at least equal to those seen with PCI and better than with medical therapy alone. Because of shortened life expectancy in the very elderly, long-term benefits of CABG as seen in younger patients may be less important, and the lower short term mortality and morbidity and shorter hospitalization may favor PCI. Importantly, quality of life, functional status, and ability for independent living need to be assessed for these patients.

Use of glycoprotein IIb/IIIa receptor inhibitors with PCI in the elderly

The benefit of glycoprotein IIb/IIIa receptor inhibitors (GPI) has been demonstrated in many studies to improve outcomes with PCI, primarily by reducing incidence of post-procedure MI. Whether this benefit extends to the very elderly has been less well studied, particularly with concern as to bleeding risks. In a series of 1,392 octogenarians having elective or urgent PCI reported by Sadeghi, et al, one-third were selected for treatment with GPI, 73% with eptifibatide. Those patients receiving GPI, compared to those
who did not, had an increase in access site bleeding with
decrease in hematocrit but no difference in need for trans-
fusion. There was an increase in incidence of GI bleeding
with GPI, but no difference in retroperitoneal bleed and
no intracranial bleeds occurred in either group. Benefit of
treatment was uncertain, Those receiving GPI had a high-
er incidence of non-Q MI but no difference in Q wave MI
or death. Those receiving GPI, however, more frequently
presented with acute coronary syndromes and required in-
traaortic balloon pump or multivessel PCI. In an analysis
of the PRISM-PLUS study, Januzzi, et al\textsuperscript{23} demonstrated
an overall increase in bleeding events with increasing age
as well as with use of tirofiban across all age groups.
However, the addition of tirofiban to heparin did not in-
crementally increase the risk of bleeding in any age group
and a decrease in ischemic events was seen with tirofiban
in all age groups. This study included very few of the
most elderly patients and there was reported to be a 1% in-
creased bleeding risk, though with no intracranial or fa-
tal hemorrhages, in the most elderly.

GPIs need to be used cautiously in elderly patients
with concern as to increased bleeding risks, though these
are rarely intracranial or fatal. Potential benefits must be
weighed carefully against these increased risks. If used,
careful attention needs to be paid to dosing, avoidance of
excessive heparin, and careful observation for evidence of
bleeding.

PCI for acute myocardial infarction (AMI) in the
Elderly

With the increasing elderly population, the inci-
dence of acute myocardial infarction (AMI) has also in-
creased. The elderly with AMI, with their greater co-
morbidities as well as advanced age, have a worse prog-
nosis regardless of treatment. As previously discussed,
worst PCI outcomes in the elderly are associated with
treatment of AMI. This does not indicate, however, that
these patients do not benefit from PCI. Outcomes from
PCI in AMI are well detailed in the review by Skelding
and Rihal in this issue of the Journal\textsuperscript{24} and will be dis-
cussed only briefly here.

In a pooled analysis of the PAMI studies from 1990-
1998, DeGeare reported that patients aged 75 and older
compared to younger patients had decreased procedural
success and less final TIMI 3 flow (85%) with increased
in-hospital mortality (10%), renal failure (4%), CVA
(3%), congestive failure (22%), and bleeding complica-
tions (18%).\textsuperscript{25} Singh, et al from the Mayo Clinic also
reported poor outcomes in patients older than 75 with
some improvement in outcomes over time though with
clinical success of only 75% and inhospital mortality of
16% in the years 1994-97.\textsuperscript{26} A series from Japan also re-
ported a high inhospital mortality rate of 8.4% in patients
older than 75 years, although if successful reperfusion (in
93% of patients, 40% with stents), mortality was only
6.6% compared to 3.0% in younger patients.\textsuperscript{27} In a se-
ries of patients older than 75 years from the Nether-
lands, de Boer reported a success rate of 90% with stents in
51% and inhospital mortality of 7% and two year mortal-
ity of only 15%.\textsuperscript{28} An Israeli study of 130 patients more
than 70 years old with 91% stent use found inhospital
mortality of 14%\textsuperscript{29} and a registry of patients older than 70
years from the GRACE study with 90% stent use reported
inhospital mortality of 13.5%.\textsuperscript{30}

Therefore, despite increasing use of stents, mortality
for PCI in AMI in the elderly remains high, the variation
among different series likely related to differences in
disease severity and patient acuity. Even with this increased
risk compared to younger patients, most, if not all data,
would indicate that outcomes with PCI are better than with
lysis in these patients. Furthermore, fewer elderly pa-
tients are unsuitable for PCI than for administration of ly-
tics. Particularly if successful reperfusion can be obtained
with PCI, short and long-term outcomes would seem bet-
ter than those with a conservative medical approach
alone. Although there are no randomized studies compar-
ing intervention vs conservative treatment in these pa-
tients, a population study of all patients admitted with
AMI in 1993-95 showed that patients aged 75-84 (only
5% having revascularization and 11% thrombolysis) had
a two year mortality of 33% while patients aged 85 or
greater (with a less than 1% use of revascularization and
3.5% thrombolysis) had a two year mortality of 53%.\textsuperscript{31}

Although the old are excluded from the majority of
randomized trials, several studies have compared PCI
with thrombolysis for AMI in the elderly. In the random-
ized Netherlands study of patients older than 75 years,
design and MI were decreased with PCI compared to lysis,
both in-hospital and at 1-2 year follow up with no differ-
ence in incidence of CVA or major bleeding complica-
tions. Goldberger, in a study of two different hospitals
using PCI or thrombolysis, found no difference in death or
MI or CVA with the two treatments though PCI resulted in
less bleeding, recurrent ischemia, and need for subse-
quent revascularization both inhospital and at 6 month fol-
low up with a reduction in reinfarction also at 6 months.\textsuperscript{32}
In the GRACE Registry study including patients older
than 70 years, there was a significant decrease in death
and MI with PCI vs lysis with no difference in other com-
lications.\textsuperscript{33} Similar to other studies, the GUSTO Iib ran-
domized study found, at hospital discharge and at six
months, an increase in death and MI with each 10 year
increase in patient age with either treatment; the com-
bined end point of death/MI/disabling stroke was significantly less with PCI than with lysis at all ages, though with no change in the incremental difference with increasing age.31

PCI for cardiogenic shock in the elderly

Patients with cardiogenic shock represent the highest risk subgroup of patients with AMI. The proportion of these patients greater than 75 years of age is increasing, ranging from 20-35% in various reported series.35-36 In the SHOCK study, which randomized patients with cardiogenic shock to early invasive treatment vs intensive medical stabilization (including intraaortic balloon pump with PCI if required a minimum of 54 hours after randomization), there was significantly increased six month survival in the early interventional approach in the overall study. However, patients older than 75 had a worse outcome with intervention with a 75% inhospital mortality and six month mortality of 80%. Other registries and single center studies, all with small numbers of patients, report much better outcomes. The Northern New England Registry series of 75 patients aged 75 and older having PCI for cardiogenic shock, had an inhospital mortality of 47% which improved with time at a rate of 30% from 1999-2000.34 In a Mayo Clinic series, with 61 patients aged greater than 75, 30 day mortality was 47%.35 Antoniucci et al with 71 similar elderly patients found a six month survival of 49%.36 In the Northern New England experience, the most elderly had comorbidities and angiographic and procedural characteristics similar to younger patients with cardiogenic shock compatible with a selection process in the very elderly. These data indicate that when elderly patients with cardiogenic shock are appropriately selected by clinical criteria, rather than by randomization, survival rates are acceptable and superior to outcomes expected from medical therapy alone.

Decisions concerning PCI in the elderly are difficult. The elderly generally, though certainly not always, are sicker with more co-morbidities than younger patients and the outcomes of PCI are worse related to these co-morbidities but also to some undefined factor accompanying advanced age. For this very reason, however, they may benefit the most from intervention. Careful clinical judgment is required to assess the likely outcome of PCI with potential risks and benefits. With appropriate selection, adverse outcomes of PCI, even in the very elderly, can be reasonably low. The elderly with AMI and cardiogenic shock represent a particularly difficult group with extraordinarily high mortality with any treatment approach. Data suggest that these patients also may benefit from emergency PCI with a high, but acceptable, risk. The greatest benefit of PCI in the elderly may be relief of angina and reduced need for medications with improvement in quality of life.

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