Lipids

These recommendations outline statin use in severe frailty. This is an evidence-informed consensus, developed in collaboration with the Dalhousie Academic Detailing Program and the Palliative and Therapeutic Harmonization (PATH) Program.

This is intended for those with severe or very severe frailty according to the Clinical Frailty Scale.

Research concludes:

- We found no studies that reported the effect of lipid lowering in severely frail older adults in primary or secondary prevention; therefore studies of the non-frail elderly that reported outcomes meaningful to the frail elderly were examined and assessed for applicability.
- We consider the following outcomes as most meaningful for the frail elderly: symptomatic non-fatal myocardial infarction (MI) (e.g., leading to morbidity such as angina or heart failure) and non fatal stroke leading to disability. The effect of treatment on mortality is difficult to evaluate with frailty (see relevant outcomes in the rationale section).
- Recommendations are intended for individuals who are ≥ 7 on the Clinical Frailty Scale (CFS). This encompasses most older adults living in long term care facilities who are typically severely frail (e.g. completely dependent for personal care). Such individuals frequently have a life expectancy of less than 2 years.

Recommendations

These recommendations consider the significant impact and decreased life expectancy of **severe frailty**.

Primary Prevention*: It is unlikely that statins provide benefit in applicable outcomes and **so there is no reason to prescribe or continue statins for primary prevention.**

Secondary Prevention*: Statin treatment in severe frailty is probably not necessary, although there may be extenuating individualized circumstances that shift the risk/benefit ratio.

With severe frailty there is:

- Uncertainty about whether statin trial outcomes are clinically meaningful.
    - For the frail elderly, an important outcome is non-fatal stroke leading to disability. However, the outcome of non-fatal stroke in some studies sometimes includes mild strokes and TIAs and the number of strokes leading to disability is not reported separately. Therefore, the outcome of non-fatal stroke might not be applicable to the frail.
    - In some statin studies, the primary composite outcome and the outcome of CHD events include those with asymptomatic heart disease such as silent MIs.
- Uncertainty about the magnitude of any benefit conferred partly because of the decreased life expectancy in severe frailty.
- Increased potential for adverse events.

Heart failure: There is evidence that statins are ineffective in improving clinical outcomes in the elderly and there is no reason to start or continue them for this indication.

Ezetimibe: There is currently no conclusive evidence that ezetimibe reduces cardiovascular events or mortality either alone or with statins in any population. There is no reason to start or continue ezetimibe for primary or secondary prevention.

Combination therapy with statins: There is no evidence of added benefit in clinical outcomes for combination therapies for either primary or secondary prevention in any population. There is no reason to start or continue other lipid lowering drugs in conjunction with statins.

Statin dosing: We suggest doses no higher than the following, and possibly lower, remembering that 2/3 of the lipid-lowering effect of a statin is realized at the starting dose. Thereafter, doubling the dose will lower LDL only by a furhter of 4% to 7%.

Atorvastatin 10mg	Rosuvastatin 10mg	
Simvastatin 20mg	Pravastatin 40mg	Fluvastatin 80mg

Adverse events: Advancing age is a risk factor for adverse effects from statins. Consider a trial of statin discontinuation if there is concern about myalgias, drug interactions, or other adverse effects.

Clinical Pearls

Doses

- 2/3 of the lipid-lowering effect of a statin is realized at the starting dose. Thereafter, doubling the dose will lower LDL by only a further 4% to 7%.
- High doses of statins are associated with increased adverse effects and uncertain benefit in the frail elderly, especially when the standard of disabling outcomes is considered.

Adverse events to statins – consider discontinuing statins

- Advancing age is a risk factor for adverse effects of statins.
- Myopathy, including myalgia (muscle pain, weakness, stiffness, and cramps) is a common adverse effect of statins. Female sex, a small body frame, frailty and multisystem diseases are some of the risk factors for myopathy.
- A meta-analysis [Richardson] did not suggest an association between statin use and cognition. However, the strength of the evidence is limited, especially for high dose statins. Case reports, retrospective cohort studies, FDA post marketing surveillance data bases and minor changes in neuropsychological testing after statin initiation suggest a possible association between statin use and cognitive decline. While these data are not definitive, a trial of discontinuation may be appropriate to determine whether cognitive impairment is statin-related.
- Avoid adding medication to treat muscular pain, cognitive impairment or diabetes until statin-related adverse events are considered.

Drug Interactions

- There are some serious drug interactions with statins. To ensure your information is current, please consult a pharmacist for potential interactions and their severity.

Lab Tests

- Regular lipid profiles should not be required since these recommendations do not support starting or maintaining statins in the frail elderly population.

- In the rare situation where statin therapy is initiated or maintained in the frail elderly the following measurements are recommended:
    - Liver enzymes: ALT (not AST) At baseline and within the first 3 months. If normal, no further testing unless symptoms develop or statin increased or switched.
    - Creatine kinase: At baseline and within 3 months. If normal, no further testing unless myalgias develop or statin dose increased or there is a switch to a different statin.

Rationale

We found no studies that report the effect of lipid lowering in severely frail older adults in primary or secondary prevention; therefore studies of the non-frail elderly that reported outcomes meaningful to the frail elderly were examined and assessed for applicability.

- Mortality: There are competing causes for mortality in the frail elderly; therefore we cannot assume that a mortality benefit shown in the non-frail population applies to frail populations. In addition, the goals of therapy may not be to prolong life in the frail.
- **CHD events:** For the frail elderly, the important outcome is symptomatic non-fatal MI (eg., leading to morbidity such as angina or heart failure.) In some statin studies, the primary composite outcome and the outcome of CHD events include those with asymptomatic heart disease such as silent MIs. Prevent asymptomatic heart disease might not prevent morbidity for the frail. Therefore, the outcome of CHD events, as reported in studies of the non-frail, might not be applicable for the frail.
- **Stroke:** For the frail elderly, the important outcome is non-fatal stroke leading to disability. However, sometimes the outcome of non-fatal stroke includes mild strokes and TIAs and the number of strokes leading to disability is not reported separately. Therefore, the outcome of non-fatal stroke as reported in studies of the non-frail might not be applicable to the frail.

We consider the following outcomes as most meaningful for the frail elderly: symptomatic non-fatal myocardial infarction (MI) (e.g., leading to morbidity such as angina or heart failure) and non fatal stroke leading to disability. The effect of treatment on mortality is difficult to evaluate with frailty.

Rationale

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