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Hemoglobin A1C also appears to be an indicator of risk for development of macrovascular disease (both CAD and ischemic stroke) in nondiabetics. Although minimal, relative risk for mortality from all causes begins to rise at HbA1C levels above 5.5 percent in a roughly linear fashion. Interestingly, those with HbA1C levels below 5 percent also appear to have a higher risk of mortality from all causes relative to those in the HbA1C 5.0 percent to 5.4 percent range. This results in a J-shaped mortality curve. Since red blood survival time affects determination of HbA1C levels, alterations in the life of red blood cells may distort HbA1C values. Rapid red blood cell turnover due to hemolysis or situations resulting in production of many new red blood cells through the treatment of anemia with iron, vitamin B 12, folic acid or erythropoietin will result in falsely depressed HbA1C levels. Recent blood transfusion and splenomegaly also may result in falsely depressed levels. Values may also be falsely high in the presence of abnormal hemoglobin (e.g., HbF or HbS). Chronic kidney disease may result in either falsely depressed or falsely elevated values.

Key points

- Mortality from all causes in nondiabetics with HbA1C levels below 6.5 percent is expressed as a J-shaped curve with increased relative risk not only for those with HbA1C levels above 5.4 percent also but also those with HbA1C levels below 5.0 percent.
- Since HbA1C quantifies glycosylation of red blood cells, alterations in red blood cell metabolism or diseases with a hematologic component may falsely skew HbA1C levels.
- Mortality causes for those having HbA1C levels below 5.0 percent have not yet been well worked out.

References