# How Does Hepatitis C Affect Non-Liver-Related Health?

And can treating the virus reduce the risk of chronic kidney and cardiovascular diseases as well as the risk of death from such causes?

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Hepatitis C virus (HCV) may be a disease of the liver, but increasingly scientists have come to understand that the virus can also have insidious effects elsewhere in the body. (These are known as extrahepatic effects because they occur outside of the liver.) For example, numerous research papers have established that hep C is associated with an increased risk of cardiovascular disease (CVD) and chronic kidney disease (CKD) as well as with being on dialysis.

Even when individuals do not have hep C, CVD is a major cause of sickness and death among those with late-stage CKD and occurs at a higher rate than among those with good kidney function. That said, in recent years, researchers have identified hep C itself as a risk factor for death among those on dialysis.

The good news is that individuals can take control of this particular risk by seeking treatment for the virus. But a key question remains: Does HCV treatment lower the risk of death among those on dialysis?

One recent paper, published in the Journal of Hepatology, analyzed data regarding more than 45,000 Swedes with hep C. Researchers found that among the 268 people who went on dialysis during the study's lengthy follow-up period, being treated for hep C was associated with a nearly 3-fold reduced risk of death compared with not being treated.

Meanwhile, the authors of a weighty new literature review and meta-analysis published in the Annals of Hepatology set out with a scientific fine-tooth comb to examine troves of available evidence backing the associations between HCV, CVD and CKD as well as to analyze HCV's apparent effect on what are known as metabolic factors, such as high blood pressure and cholesterol.

Scouring databases of published research covering 1989 to 2016, the researchers conducted a meta-analysis of 14 observational studies including some 145,000 people on long-term dialysis. They found that being HCV positive was an independent risk factor for death among this population; specifically, hep C was associated with a 1.35-fold increased mortality risk. The

researchers could not determine, however, whether this higher risk of death was driven only by liver-related deaths. They did, nevertheless, find that among all those on dialysis, individuals with hep C had a 3.8-fold increased risk of liver-related death.

Additionally, after adjusting their data for various factors, the study authors found that among all those on dialysis, having HCV was associated with a 1.21-fold increased risk of death from CVD.

The authors of the new paper theorized that the increased CVD risk among those on dialysis may result from insulin resistance, non-alcoholic fatty liver disease (NAFLD) or inflammation driven by the virus. Insulin resistance and NAFLD in particular may give rise to various components of metabolic syndrome (itself a CVD and CKD risk factor), including high blood pressure and irregular blood lipids, such as cholesterol.

Researchers behind a recent meta-analysis of 22 observational studies of 730,000 people adjusted their data for various factors and found that having hep C was associated with a 1.65-fold increased risk of dying from CVD, a 2.27-fold increased risk of developing plaque in the carotid arteries and a 1.3-fold increased risk of stroke.

It's important to consider, however, that because the studies analyzed here are observational—they are not based on a randomized design—it is harder to ultimately determine a likely cause and effect between HCV and a particular health outcome based on their findings. Even when the researchers adjust their data to account for differences between individuals, it is possible that there are non-HCV-related variables that are more common among those with the virus and are actually the key drivers of these health problems.

That uncertainty notwithstanding, the study authors stress that conventional risk factors for CKD in particular, including aging (25 percent of those older than 65 in Western nations have the disease), diabetes, high blood pressure and metabolic syndrome, do not completely explain why people with hep C have a higher rate of CKD.

Recently, scientists have indeed found evidence that hep C is an independent risk factor for kidney disease. For example, the authors of the new paper conducted a meta-analysis of nine studies including nearly 2 million individuals and found that having HCV was associated with a 1.43-fold increased rate of CKD diagnosis.

These scientists also reviewed available scientific literature to investigate HCV's relationship with diabetes. In one long-term study of nearly 5,000 individuals in Taiwan, researchers found that having the virus was associated with a 1.7-fold increased risk of diabetes. This independent relationship between HCV and diabetes was particularly strong among those who were younger or had a higher body-mass index (BMI). In a promising sign, those who were treated for hep C saw their insulin resistance (a major factor of diabetes) decline both during and after treatment.

So what does the medical literature say about how hep C treatment may affect other non-liver-related health and survival factors?

For starters, a retrospective study of about 200 people with hep C in Taiwan who were followed for a median of nearly five years indicated that treatment for the virus lowers the risk of stroke by 61 percent—a figure the authors arrived at after adjusting their data to account for other stroke risk factors.

In an analysis of five studies investigating the impact of hep C treatment on the progression of CKD, researchers found that such treatment may indeed lower the risk of death related to kidney disease. One study included about 12,000 Taiwanese people treated for HCV who were matched one to two with nearly 25,000 people with hep C who went untreated for the virus. The study's authors calculated that over an eight-year period, the proportion of the treated and untreated groups that developed end-stage kidney disease was a respective 0.15 percent and 1.32 percent.

After adjusting the data for various factors, the investigators behind the Taiwanese study found that hep C treatment was associated with an 85 percent reduced risk of end-stage kidney disease as well as a 23 percent reduced risk of acute coronary syndrome (sudden blockage of blood flow to the heart) and a 38 percent reduced risk of stroke.

Another study conducted in Taiwan found that hep C treatment was associated with a 58 percent reduced risk of developing CKD.

Ever-accumulating evidence aside, scientists have not been able to prove definitively that hep C causes CKD progression and CVD. Nevertheless, as the authors of the new paper point out, considerable evidence suggests that people living with the virus should be screened for CKD even if they don't have traditional risk factors for that condition.

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