Pneumonia hospitalisation associated with long- and short-term risk of cardiovascular mortality

COVID-19 and non-COVID-19 pneumonias in people with type 2 diabetes are both associated with significantly increased risk of mortality from cardiovascular disease (CVD), according to this nationwide, prospective cohort study from Scotland published in *Diabetes Care*. CVD mortality risk was initially much greater in the first 30 days post-exposure in people with COVID-19 pneumonia; however, beyond this time the risk levelled out to a similar rate as with non-COVID pneumonia, with around a fourfold increased risk in both pneumonia types. Hospitalisation for any type of pneumonia should, therefore, be seen as a significant risk factor for future CVD death, and care should be taken to optimise known cardiovascular risk factors, such as blood pressure, lipids and glycaemia, in these individuals. Adhering to recommendations on pneumococcal and COVID-19 vaccination in people with type 2 diabetes should help reduce future pneumonia burden and, hence, reduce associated CVD mortality.

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People with cardiovascular disease (CVD) and people with type 2 diabetes have increased risk of pneumonia and are at greater risk of hospitalisation and mortality from COVID-19 than those without these conditions. Previous studies, including the Veterans Affairs database study reported in *Diabetes Distilled* previously (Xie et al, 2022), have demonstrated significantly increased risk of CVD, in both the short and long term, in those requiring hospitalisation for COVID-19 pneumonia. In the present study, published in *Diabetes Care*, McGurnaghan and colleagues sought to identify whether the CVD mortality risk following COVID-19 pneumonia was higher than that following other types of pneumonia.

The SCI-Diabetes study

The researchers used data from the comprehensive SCI-Diabetes (Scottish Care Information – Diabetes) database, which includes information from primary, secondary and community care and retinal screening for over 99% of people diagnosed with diabetes living in Scotland. Using a unique health service identifier for each person, hospital admissions and mortality data are linked to the SCI-Diabetes database. Two cohorts were identified:

- Those with type 2 diabetes in the 4 years prior to the pandemic (*N*=263 922; follow-up almost 1 million person-years).
- Those with type 2 diabetes in the period of January 2020 to end of November 2021 (*N*=284 801; follow-up 515 226 person-years).

People who had been admitted to hospital for bacterial or viral pneumonia in the 3 years before each timeframe were excluded. Hospital admissions with bacterial or viral pneumonia or with COVID-19 pneumonia were included and, where there was any evidence that COVID-19 or a positive test during admission was involved, they were included in that group for the analyses. CVD mortality coded anywhere on the death certificates was included.

Remaining data were gathered from SCI-Diabetes, with the most recent data used and a maximum look-back of 3 years for most parameters or 10 years for prior CVD, immune disease, chronic kidney disease, asthma, liver disease and neurological diseases.

Results

People with type 2 diabetes who developed pneumonia were older, more likely to be smokers, had greater social deprivation, had more

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Diabetes & Primary Care **26**: 105–7

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comorbid conditions including CVD, and were on more therapies than those who did not develop pneumonia, highlighting the importance of adjusting for confounders. Those who developed non-COVID pneumonia were, on average, older than those with COVID-19 pneumonia and had more comorbidities.

After initial adjustment for age, sex and diabetes duration, both types of pneumonia were associated with a 10-fold greater risk of CVD mortality than in those without pneumonia. After adjustment for further confounders, the risk was slightly higher for COVID-19 pneumonia than non-COVID pneumonia (rate ratio [RR] 9.13 vs 7.30 compared to those without pneumonia). Similar ratios were found when analysis was restricted to those without previous CVD.

Looking only at the period beyond the first 30 days following either type of pneumonia, the risk was lower for both groups, with an RR of 3.35 for COVID-19 pneumonia and 4.24 for non-COVID pneumonia. When all-cause rather than CVD mortality was examined, the RRs were similar, and again people with COVID-19 pneumonia had higher initial mortality but then slightly lower mortality after the first 30 days compared to those with other pneumonias.

Discussion

This study found that pneumonia of any type was associated with both short-term (<30 days) and longer-term risk of CVD mortality. In the first 30 days post-infection, this risk was higher in those with COVID-19 pneumonia than for other types of pneumonia; however, after 30 days the risks were similar, with a greater than 4-fold increased risk of CVD death in both groups compared to those without pneumonia.

In the pre-pandemic cohort, when fully adjusted for CVD risk factors, non-COVID pneumonias were associated with a 5.5-times elevated risk of cardiovascular death, and this risk increased further (RR 7.3) during the pandemic. Failure to recognise this increased risk during the pandemic may have amplified the previous concerns of the (likely direct) long-term impact of COVID on CVD mortality.

Although COVID-19 pneumonia was associated with a more than 9-fold increased risk of CVD mortality overall – higher than with other pneumonias – the increased risk was mainly during the first 30 days post-exposure, beyond which it equalised with that following non-COVID pneumonia over the average follow-up of 21 months.

The mechanisms driving the increased CVD risk can only be postulated at present. The authors speculate that systemic inflammation, myocardial damage during the infection and/or persistent thrombogenesis effects may be involved. Early greater increases in CVD mortality following COVID-19 pneumonia are consistent with the increased systemic inflammation and haemostatic conditions seen with COVID-19 compared with other infections. Until more is known, we are unable to directly influence the underlying mechanisms, and all that can be targeted are conventional CVD risk factors.

Study strengths and weaknesses

Strengths of the study include the comprehensive type 2 diabetes and mortality data from everyone with diabetes in Scotland, the comparison of the relative risks in those with COVID-19 pneumonia and other types of pneumonia (both before and during the pandemic) and the similar pattern observed for all-cause mortality. Since this was a cohort study, it is impossible to rule out unknown confounders in both groups; however, the persistence of the findings after extensive adjustments for known risk factors means it is unlikely that confounding explains all the increased CVD risk.

Such studies rely on accurate coding of pneumonia types. Collider bias (see Sterne, 2020, for an explanation) due to hospitalisation may have affected the <30-day data for both types of pneumonia but is unlikely to have impacted the >30-day data. The focus in this study was on people hospitalised for pneumonia, as this was likely to be more accurate than positive PCR testing, since around one third of people had asymptomatic COVID-19.

Implications for practice

This study suggests that the long-term, direct detrimental effect of COVID-19 infection on CVD mortality rates may be less than previously

believed, and comparable to the risk following other types of pneumonia. Nonetheless, it reminds us of the importance of identifying people who are hospitalised with any type of pneumonia and being aware of their significantly increased risk of cardiovascular death, both in the short and longer term, whether or not they have had previous CVD events.

As with all other searches, finding these people at high CVD risk depends on the quality of our original coding. Reviewing pneumonia coding in my own practice, it is not easy to identify those who were hospitalised with COVID-19 pneumonia, as admissions were coded in different ways due to the huge workload pressures at the time. Likewise, only a very small number of people with type 2 diabetes have been coded with pneumonia of any type (SNOMED code 233604007), so it is not clear if all such admissions have been captured. It is, therefore, useful to ask about hospitalisation for COVID-19 or other types of pneumonia in consultations with people with type 2 diabetes, and to code previous events opportunistically.

For all historical and new pneumonia cases identified, we should aim to reduce future CVD risk. Are blood pressure, lipids and glycaemia optimised, and has the person received advice and support for smoking cessation where appropriate? Has their high risk of CVD resulted in treatment with an SGLT2 inhibitor and/or GLP-1 receptor agonist with evidence of CVD benefit, to further reduce that risk? Has everyone with diabetes had pneumococcal and appropriate COVID-19 vaccinations to reduce the future risk of pneumonias?

This is another wonderful opportunity to make every contact count and reduce the risk of CVD events and mortality. Let's find these people and help them optimise their CVD risk! ■

McGurnaghan SJ, McKeigue PM, Blackbourn LAK et al; Scottish Diabetes Research Network Epidemiology Group (2024) Impact of COVID-19 and non-COVID-19 hospitalized pneumonia on longer-term cardiovascular mortality in people with type 2 diabetes: A nationwide prospective cohort study from Scotland. *Diabetes Care* 18 Jun [Epub ahead of print]. https://doi.org/10.2337/dc24-0124

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Impact of COVID-19 and non-COVID-19 hospitalized pneumonia on longer-term cardiovascular mortality in people with type 2 diabetes: A nationwide prospective cohort study from Scotland

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