At-home testing for heart failure, transplant patients: Can it work?

David Wild

January 2019—Medicare hospital readmission rates are down under the Centers for Medicare and Medicaid Services readmissions reduction program, though hospitals are still paying millions in penalties, in part because new conditions are included in the calculations. Can at-home self-testing of some patients bring readmission rates down further, not only to save dollars but also to keep patients healthier and in their homes, to increase access to care, and for a better patient care experience?

That's the question Robert Nerenz, PhD, explored in his talk at last year's AACC annual meeting, in a session on enhancing patient care using point-of-care testing. "Atypical point-of-care testing might be able to meet some of the country's health care challenges," said Dr. Nerenz, assistant director of clinical chemistry at Dartmouth-Hitchcock Medical Center and assistant professor of pathology and laboratory medicine, Geisel School of Medicine at Dartmouth. Although cost savings are an important element, what interests Dr. Nerenz most about at-home testing is patient health. "Presumably," he said, "if you're not being admitted to the hospital, you're doing better."

At-home testing "is already kind of creeping into our standard of care," he said, but "when we talk about expanding this, particularly to a fingerstick specimen, there are lots of concerns that people rightly have."

Specimen quality is one. "We know that a fingerstick specimen is not as good as a venous specimen or arterial specimen. We know there's tissue fluid in it, and there are a number of other concerns," among them how accurate the value is once the specimen is applied to the instrument.

"How can we train people who don't have a formal lab background to do this testing properly or at all the prescribed testing intervals? And does any of this matter? Is there a positive impact on patient care?"

In the first of two examples, Dr. Nerenz zeroed in on patients with congestive heart failure. A study published in *JAMA* (Felker GM, et al. 2017;318[8]:713–720) examined whether an NT-proBNP-guided treatment strategy improves outcomes versus usual care in high-risk patients with heart failure and reduced ejection fraction. The treatment goal in the study was to keep NT-proBNP below 1,000 pg/mL, measured in a laboratory.

The authors randomized almost 900 patients to undergo NT-proBNP-guided treatment or to receive the usual care in accordance with the guidelines, with emphasis on titration of neurohormonal therapies for HF. Serial measurement of NT-proBNP was discouraged. The NT-proBNP-guided therapy was not found to be more effective.

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While a number of reasons might account for the lack of a difference, one point the authors made was that NT-proBNP was measured only "every couple of weeks, every month, every six weeks," Dr. Nerenz said. The authors of a subsequent study, noting that infrequent measurement potentially underestimates the benefits of serial NP testing to guide treatment decisions, examined whether daily at-home measurement could be an alternative (McDonald K, et al. *Eur J Heart Fail.* 2018;20[3]:474–480).

While at-home fingerstick measurement of BNP means "stepping away from a pristine venipuncture specimen measured in a central lab toward a less perfect specimen measured on a slightly less accurate instrument," Dr. Nerenz said, "what we gain is real-time information and more data points collected every single day."

Generally, heart failure patients are advised to monitor their weight and symptoms. Patients in the at-home study were instructed not only to weigh themselves but also to measure their BNP each day using the Alere Heart Check system. They were asked to do so at the same time each day, before eating breakfast and before taking morning medications. Researchers examined the participants at one, three, and six months after trial outset, or at the time of study withdrawal.

Of the 107 patients monitored in the study for a median of 172 days (whose left ventricular ejection fraction was less than 40 percent), 35 had their treatment guided by daily BNP and weight values, and 34 patients had treatment guided by weight but not BNP. Thirty-eight participants had treatment blinded to both values.

"A key point in this study," Dr. Nerenz said, "was that both BNP and weight values automatically went into a central database where researchers could then look at them."

"And in their infinite wisdom, these authors said, 'We know there may be some inaccuracy with the individual data points. What we really care about is the trend. So let's look at a six-day moving average.'" Is BNP going up or down or staying the same? "By looking at the aggregate of six points," Dr. Nerenz said, "some of that individual error will now start to normalize out. And so they asked, 'Does the BNP trend predict decompensation?'"

Dr. Nerenz provided a look at three patients. One patient had BNP levels around <100 pg/mL until day 125, before which there were modest fluctuations from day to day but BNP was not increasing. "Presumably, that patient's heart is not super stressed," he said. After day 125, BNP values for this patient began to rise, and within 15 days were about 10 times higher, at which point the participant was hospitalized for acute decompensated heart failure.

While weight rose along with BNP values in the period immediately preceding heart failure, it also increased between days 80 and 100 and between days 20 to 40 with no corresponding increases in BNP and no need for hospitalization or clinic visits. "So at least in this particular patient, it appears that BNP is a more specific predictor of decompensation than is weight gain," Dr. Nerenz said.

A second patient had BNP values steadily decline from greater than 500 pg/mL at baseline until day 40, when they began to rise, and the patient was ultimately hospitalized on day 65 for acute decompensated heart failure. "In this patient, there was a slightly different pattern but the same basic take-home message." Although values in weight gain and BNP "pretty much parallel each other" during the period before hospitalization, "if we go all the way back to day zero [up until] day 30, BNP is trending down while weight is trending up. So again weight appears to be a slightly misleading, or at least a nonspecific, indicator," he said.

The third patient's BNP values were elevated at the start and declined steadily over the first 60 days of monitoring, falling from greater than 1,000 pg/mL and stabilizing at less than 100 pg/mL, but body weight rose steadily during the same period. This patient did not experience acute decompensated heart failure or require IV diuretics during

the monitoring period but was hospitalized for vasovagal syncope.

In sum, a univariate analysis found that every 2.7-fold increase in the natural log of the six-day moving average of BNP leading up to the time of hospitalization or cardiovascular death was associated with a 2.2-fold increase in the risk of such an event (hazard ratio 2.2; 95 percent CI 1.48–3.34).

“If we look at the univariate models, the hazard ratio indicates weight gain is actually a stronger predictor of poor outcomes than BNP, but the 95 percent confidence interval is very wide,” Dr. Nerenz noted (HR 3.22; 95 percent CI 0.97–10.71). “We really don’t know. It could be a very poor predictor with a hazard ratio less than one, all the way up to a very strong predictor with a hazard ratio of 10.7.”

However, in a multivariate analysis, the authors found the six-day moving average of BNP, when adjusted for the patient’s initial BNP value, was a stronger predictor of a primary event than weight gain with a narrower confidence interval (HR 3.27; 95 percent CI 1.84–5.83).

They concluded that BNP home testing is feasible and that in this patient group, “given adequate training,” Dr. Nerenz said, individuals can perform home BNP testing. “And, relative to weight gain, the adjusted natural log of the six-day moving average seemed to be a stronger predictor of poor outcomes.”

Research is needed to determine the most accurate alert criteria for this patient population, Dr. Nerenz said. “If we’re going to use this to intervene in patients and be more aggressive with their treatment to prevent hospitalization, what are the cues that stimulate us to do that?” And the critical question: Are outcomes better? “That’s the next step that’s required for at-home BNP measurement,” he said.

Dr. Nerenz moved to a different patient group: kidney transplant recipients. A study conducted at Leiden University Medical Center in the Netherlands looked at at-home monitoring for these patients. It examined whether transitioning creatinine and blood pressure testing into the home can lead to earlier detection of rejection, reduce the number of outpatient visits, and “make patients more active players in their care,” Dr. Nerenz said (Van Lint C, et al. *J Med Internet Res.* 2017;19[9]:e316).

Participants were asked to monitor their creatinine levels daily for four weeks, every other day in weeks five to nine, twice weekly in weeks 10 to 15, and weekly from week 16 onward for the duration of the one-year study. They used the Nova Biomedical StatSensor Xpress-i Creatinine Meter and were given a blood pressure self-monitoring device. They were instructed in how to use the devices, how to manually register their creatinine values in an online system that physicians could also access, and how to respond to feedback from the system. Fifty-eight patients were supplied with devices; four never performed any measurement.

To provide feedback to patients, the system compared the most recent creatinine value to the mean of the five previous values. If the registered value was less than 15 percent higher than the mean of the five previous values, patients were given a “green light” and asked to continue with their current testing schedule. If the value was 16 to 20 percent higher, they were given an “orange light” and asked to repeat their measurement, and if the value was more than 20 percent higher, they were advised to seek care.

The key difference between this study and the heart failure study, Dr. Nerenz pointed out, is that the transplant recipients didn’t have automatic data upload. “Patients were responsible for doing the testing and then manually entering the information into a study database. And so the question here is, Is this feasible?” The finding: “Patients were much better at performing the measurements than they were at registering” the results, said Dr. Nerenz.

The study also addressed whether the data are sufficiently accurate to make clinical decisions. The authors examined this by comparing the accuracy of results using the POC method from a fingerstick with a concurrently collected venipuncture specimen tested in the central lab. Using a total allowable error of 6.9 percent, they found that many points fell outside the allowable error.

“So you could say, well, that’s it. It’s not sufficiently accurate. This is not going to work. But the authors point out that, similar to the BNP study, we know the individual data points are not going to be as accurate. We’re not

contesting that point," he said. "What we want to know is, What's the trend? Is creatinine going up or down?"

The authors found disagreement on each day of testing, "but the trends are the exact same. When it goes up on one method, it goes up on the other, and vice versa," Dr. Nerenz said.

How well did patients follow the feedback provided to them through the online system? Of 258 requests the system provided to patients to perform a repeat measurement, only 53 percent of those were followed. Of the second measurements that were performed, 39 got an orange light and a request to perform another measurement the next day, and 85 percent of those requests were adhered to. Finally, of 24 requests to contact the hospital, only 58 percent were adhered to.

"So the authors quite rightly were concerned by this and they thought, 'Why aren't these patients doing what the system is telling them to do?' And what they realized is that these non-adherence episodes were due to delayed registration," Dr. Nerenz explained. "If a patient got a creatinine value on Monday that would say, 'do another measurement' or 'go to the hospital,' but they didn't log that in the system until Friday, they're going to say, 'That's old news. I don't have to act on that.' So it kind of gets back to manual entry versus automatic data entry."

To assess how accurately the patients entered data, the authors compared 3,963 measurements logged into the device to values registered online on the same day and found that 3,448 (87 percent) were registered correctly, while 515 (13 percent) were incorrect.

"But what I find most interesting is there were about 1,300 unregistered measurements"—measured values that were never entered into the online system. Six hundred ninety-one (54 percent) were omitted, and 600 (46 percent) were unselected. In the latter case, "these are values where a patient was instructed to do one measurement and did two or three or four and had multiple different values to pick from but selected one of those values for upload and then the others were not uploaded."

When the authors compared the mean values of selected and unselected measurements, they found the omitted values were significantly higher than the registered ones, suggesting patients tended to make their kidneys "look best," Dr. Nerenz said, adding, "I think automatic data upload is a necessity."

As with the BNP study, he said further research is needed to define the optimal alert criteria and to determine whether at-home creatinine testing improves patient outcomes. "There are some ways that this [at-home testing] can go wrong . . . but, by and large, I think this has definite potential."

To be implemented successfully, he said, these devices should require minimal training, testing has to be convenient for the patient, and results have to be accurate. "But we know there are going to be inaccuracies if we compare single data points generated at home versus single data points generated on a venipuncture specimen in the lab. But I would argue that's okay because we're gaining real-time information that we can use to trend patients, as opposed to gaps in information because we're only testing once a week or once a month or every six months, or whatever it may be."

Automatic data reporting is a must, he repeated. "Manual entry is not a viable solution." And the data have to be actionable: "There has to be something we can do to intervene. If there's no treatment we can offer the patients, there's no point in doing any of this."

Brenda Suh-Lailam, PhD, DABCC, director of clinical chemistry and point-of-care testing and director of quality, Department of Pathology, Ann and Robert H. Lurie Children's Hospital of Chicago, and assistant professor of pathology, Northwestern University Feinberg School of Medicine, said in the same AACC session and in a recent interview that the use of at-home testing devices on inpatients, when they're brought into the hospital, is one of the POC testing challenges laboratories will face in the future. There are no guidelines, for example, on how to manage results from inpatients with continuous glucose monitors.

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—Brenda Suh-Lailam, PhD, DABCC

“Should the results be downloaded into the patient’s electronic medical record while they are an inpatient?” she asks, adding that policies for such are needed. “Do laboratorians need to validate or calibrate at-home devices? Will they need to ensure quality throughout inpatient CGM use?” And “what is the laboratory’s responsibility for training and troubleshooting related to at-home device use?”

A panel of 27 experts in hospital medicine and endocrinology in 2015 discussed the current and potential future roles of CGM in the hospital (Wallia A, et al. *J Diabetes Sci Technol.* 2016;10[5]:1174–1181). They concluded, Dr. Suh-Lailam says, that it has the potential to provide useful information and improve care in ICU and non-ICU settings and that there is a role for continuing the use of home CGM in the hospital, but that the cost and lack of outcome data limit widespread adoption. Whether there is a role for laboratorians in this setting is still an open question, Dr. Suh-Lailam says.

To illustrate the challenges related to at-home device use—in this case a ketone meter—in a hospital, Dr. Suh-Lailam shared a case in which a patient with glycogen storage disease type IIIa was scheduled for a four-day inpatient diet treatment to begin in eight days at her institution. Ketone and glucose checks were needed every one to two hours to monitor treatment efficacy.

“The problem was that we were not yet offering ketone testing in our laboratory, so the clinical team was wondering if they could use the patient’s ketone meter since testing was required so often,” she said. “However, the problem with using the patient’s meter is that its performance has not been validated for use in our hospital, so clinical decisions cannot be made using that device. We had to come up with a quick way to provide ketone results during this patient’s hospital stay.”

Purchasing and validating a POC testing device on short notice is a challenge, she says, as is training personnel on different shifts. “We decided to take on the challenge and we were fortunate to have vendors that were willing to work quickly with us to provide us with a hospital-grade point-of-care testing device, which we validated.”

“Personnel were trained and some then received additional training to be able to help train operators on other shifts. The success of this project was due to the collaboration between the lab, clinical team, and vendor,” she says.

A poll of attendees in the AACC session found that more than 80 percent said more POC testing is being done in their institutions compared with five years ago. Many said their institutions were acquiring, or recently acquired, a

new POC testing device not used previously in their institutions. More POC testing to manage different disease states and more testing in nontraditional settings is what the future of POC testing will look like, Dr. Suh-Lailam says. And that includes more such testing in assisted-living and nonmedical facilities and, yes, the home.

“We seem to see more and more of the same kind of pattern,” Dr. Nerenz said, “where point-of-care testing continues to expand into areas beyond the traditional health care settings—outside the hospital, outside outpatient clinics.” If at-home patient self-testing “explodes,” he asks, “how can we insert ourselves into the discussion to make sure it’s done appropriately, correctly, and safely?”

David Wild is a writer in Toronto.