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To Wear a Mask Is to Be Brave. To Trust Your Doctors Is to Be Brave

By Abubakr Chaudhry, MD

The pandemic is a lie. I will not wear someone else's fear. This is all fake news. It is remarkable to see these statements littered across the news and social media. Individuals with a fairly decent level of understanding and intelligence pandering to these ideas just go to show how strong anti-science culture has become.

On January 19, the first American would test positive for the novel coronavirus. By early February, the hysteria would start to set in and social media would start increasing speculative reporting. By late February, the stress and arguments about who should take responsibility began to boil over. Then there was the increase in fear among healthcare exposure rates, conflicting case fatality reports, and frustrations with the CDC on the flip-flopping in guidelines.

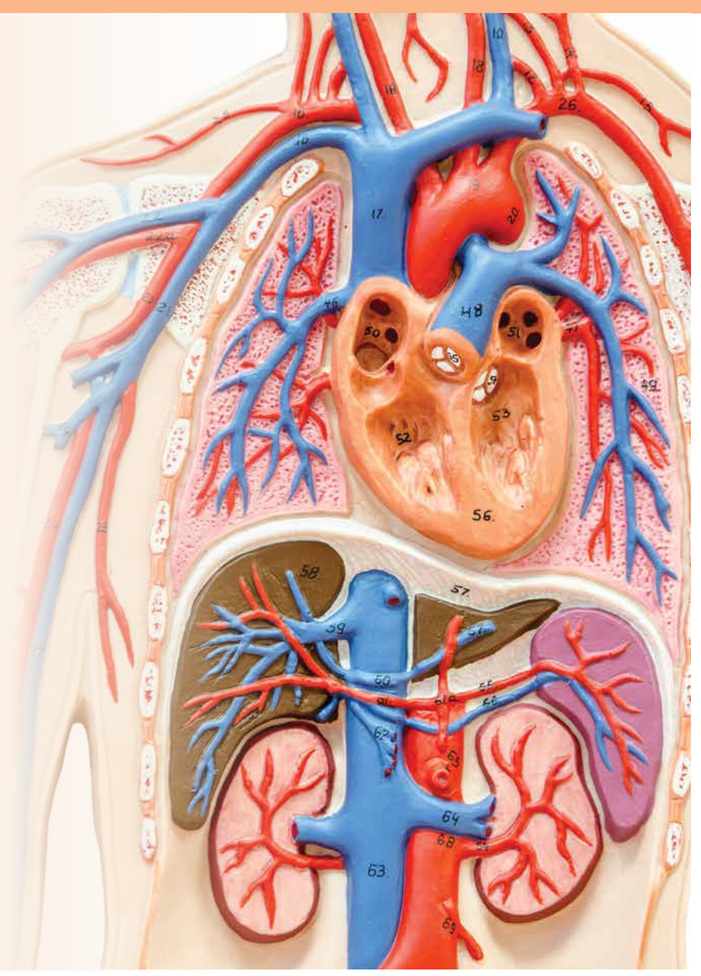
We became tired of the complaining, fear, and misinformation, so we decided to pen a guideline for our hospital. Georgia went on lockdown April 3. Throughout March and April, the world seemed to trust us as the scientific community to lead them through this crisis.

By April, we saw our algorithms were working, and we had some of the best outcomes in the state. People were adhering to the guidelines by staying home. Businesses had shut down, the spread was contained, and we could see the light at the end of the proverbial tunnel. Then, on April 24—with 892 deaths and 22,147 infected in GA—the lockdown restrictions were eased in our state. We were one of the last to close but the first to reopen. We knew the world needed to open; we just didn't know our world would open like this. I remember wondering why we couldn't mandate masks, contact tracing, and social distancing when we reopened. The virus became political.

When I started writing this, I was upset at a social media comment I read from a friend that read, "This pandemic is a joke, I will not wear a mask because I will not wear their fear." Now, I see that he was afraid and uninformed. People, in general, are still afraid, if not of the virus, then of loneliness, poverty, or even subjugation. When people exhibit these fears, and if their voices are loud, the politicians must bend to their will. If our politicians are afraid and their voices alleviate our fears, then we bend to *their* will. My point is, it is OK to be afraid. I am a pulmonary and critical care doctor, my wife is a pediatric intensivist, we have a small child, and we are afraid. But to wear a mask is to be brave. To social distance is to be brave. To trust your doctors is to be brave. To those with doubts, know that you are correct in your feeling that the system is broken. I don't know how to fix it, but I know that it has to be done soon. Help us get through this so we can build a better world: a world built from understanding, not from fear.

Abubakr Chaudhry, MD is a pulmonary and critical care physician.

Combining Hematologic & Organ Responses to Predict Outcomes in AL Amyloidosis



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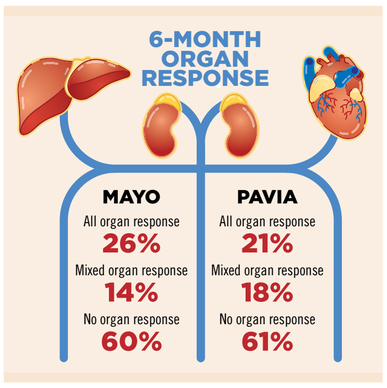
Evidence indicates that light chain (AL) amyloidosis is caused by deposition of abnormally folded light chains in organs like the heart, kidney, liver, and nerves. These abnormal light chains are secreted by plasma cells and often lead to involvement of more than one organ in a given patient. Organ damage is the main driver of morbidity and the leading cause of early death in such patients. Treatment in patients with AL amyloidosis is targeted toward the underlying plasma cell clone. The objective of treatment is the rapid reduction of circulating light chains to stop further organ damage and allow for gradual degradation of the organ amyloid deposits, resulting in organ improvement. While both hematologic and organ responses are important in AL amyloidosis, there has been no model to concurrently assess both hematologic response and individual organ responses for a given patient and compare these across patients receiving different treatments. We and our colleagues sought to fill this gap, to develop a system that can be used in the clinic to assess the impact of therapy, as well as provide a framework for regulatory purposes for drug approvals.

For this study, published in *Blood Cancer Journal*, we developed a composite model that can allow for both hematologic and organ response assessment in patients with AL amyloidosis. To develop this model, we assessed outcomes with treatment in two large independent cohorts of patients with newly diagnosed AL amyloidosis. The testing cohort included 473 Mayo Clinic patients, and the validation cohort included 575 patients from the Amyloidosis Center in Pavia, Italy. The majority of patients in both cohorts had cardiac involvement, and about one-half had involvement of more than one major organ (heart, kidney, liver). Response assessment was conducted at 6 months from the start of treatment. As there was no existing model to evaluate multiple organ responses simultaneously, we first developed a combined parameter to assess organ response across multiple organs. Using existing criteria for individual organ responses, organ response was classified as one of the following:

- All organ response – response in all of the involved and evaluable organs (heart, kidney, liver).
- Mixed organ response – response in at least one of the organs
- No organ response.

Key Findings

The rates of combined 6-month organ response in the Mayo and Pavia cohorts were:



As expected, the combined organ response rates increased with deeper hematologic response. In patients achieving a complete hematologic response, response in all organs was seen in 35%-38% of patients, compared with 26%-30% in patients achieving very good partial response and 16%-21% in those with partial response. In both cohorts, patients who achieved response in all organs had significantly better overall survival outcomes compared with those achieving response in some or none of the involved organs.

Each patient was assigned a score for their combined organ and hematologic responses. Scores for hematologic response varied from 0-3, with 0 representing complete response, 1 representing very good partial response, 2 representing partial response, and 3 representing no response. Scores for organ response varied from 0-2, with 0 representing all organ response, 1 representing mixed response, and 2 representing no response; lower scores indicated better response. We estimated survival outcomes of patients with different scores (1-5) relative to a score of 0, which indicated complete organ and hematologic response. Using these scores, we developed a composite model with which patients could be divided into two main groups based on similar outcomes for survival. Group 1 included those with scores of 0-3, and group 2 included those with scores of 4-5. In the Mayo cohort, group 1 had significantly better survival outcome compared with group 2 (median overall survival, not reached vs. 34 months) with a hazard ratio (HR) of 3.4 (95% confidence interval [CI]: 2.5-4.6). This model was then validated in the Pavia cohort, in which median survival in group 1 was 87 months, compared with 23 months in group 2 (HR, 2.8 (95% CI, 2.2-3.5).

Looking Ahead

The composite model performed better for predicting survival than using hematologic response or organ response alone. As this model was predictive of survival, it may be used as a surrogate endpoint for treatment in clinical trials, allowing for rapid assessment of treatment outcomes. This model can also allow us to compare outcomes of patients with different treatments. Future studies using this model are needed to evaluate the utility of changing treatment based on early composite response assessment.

33 CHARTS

Refusing Telemedicine – Can Patients Opt-out of Remote Care?

With the sweeping rise of COVID-19, telemedicine has taken healthcare by storm. During the local surges, this served as a mandated way of maintaining safe distancing. But as things come back to a new normal and as we decide where telemedicine fits in to a clinic structure, it might be worth asking: should patients have the option for in-person care? Is refusing telemedicine in favor of being physically seen a choice patients should be able to make? As we begin to settle in to a fixed role for telemedicine in the post-COVID world, centers are beginning to shape processes around telehealth.

Three assumptions that we make about patients and virtual encounters give shape to our policies:

ASSUMPTION OF APPROVAL

We assume that telemedicine is what patients prefer. The belief that patients prefer to be cared for in the context of their home isn't always the case. There may be sensitive issues or a hidden agenda that doesn't show well across a screen.

ASSUMPTION OF EQUIVALENCE

We assume that telemedicine is as good as in-person care. There is a bias to try to assess virtually some conditions that may best be assessed in real life. But, sometimes, medicine needs to be inconvenient.

ASSUMPTION OF CAPACITY

We assume the patient is able to participate in a virtual visit. Some families lack Internet access and equipment to complete a telemedicine visit. Tech insecurity is a bigger issue than thought initially when we started doing telemedicine.

There are many reasons why a patient may prefer an in-person visit. Our assumptions about the magic of telemedicine are not always right. While we should work to accommodate the preferences of the patient, patients need to understand that there are conditions and circumstances where an in-person visit is not necessary. And patients should be offered the right of refusing telemedicine.

Will our telemedicine policies pull us back to an imbalanced doctor-patient relationship? After the COVID dust falls, we need to create more structure that respects the interests and will of the patient. Telemedicine is a moving target. What works or doesn't work today may have a very different solution or experience a year from now. Flexibility and rapid reiteration of our processes will be critical to successful adjustment and growth.

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Understanding Allogeneic HCT Survival Risks

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Despite numerous studies assessing potential improvements in treating myelofibrosis, allogeneic hematopoietic cell transplantation (HCT) remains the only treatment option with the potential for a cure. However, HCT brings with it risks of morbidity and mortality, explains Tania Jain, MBBS. "It would be helpful to understand which patients are at an increased risk of relapse or death," she adds. For a study published in the *Blood Cancer Journal*, Jain and colleagues sought to determine the factors that influence post-transplantation outcomes to identify patients, early in the course of the HCT, who are at high risk for morbidity and mortality.

The researchers studied factors at day +100 post-transplantation that had a potential of predicting worse outcomes. The team conducted a retrospective chart review to gather baseline data on patients, disease- and HCT-related data, day 100 characteristics, and post-HCT outcomes. Information collected included molecular mutation status, bone marrow fibrosis, spleen size, donor chimerism, presence of any grade of acute graft versus host disease (GVHD), and red blood cell (RBC) and platelet transfusion dependence. Data were then used to understand differences in survival by calculating individuals' risk factor counts.

RBC transfusion dependence (HR, 9.02), platelet transfusion dependence (HR, 8.17), 100% donor chimerism in CD33+cells (HR, 0.21), unfavorable molecular status (HR, 4.41), normal spleen size (HR, 0.42), grade 2 or greater bone marrow fibrosis (vs. grade ≤ 1; HR, 2.7) and poor graft function (HR 2.6) at day 100 were statistically significantly associated with relapse-free survival. RBC transfusion dependence and unfavorable molecular status (defined as less than 100% donor chimerism in CD33+ cells or presence of detectable driver mutation on next generation sequencing testing) at day +100 were statistically significantly associated with inferior relapse-free survival, in the multivariate analysis. "Interestingly, the degree of marrow fibrosis at day +100 was not significantly correlated with outcomes," adds Jain.

"This is only a first step that has helped us identify those high-risk patients," notes Jain. "Additional studies analyzing post-transplantation strategies could help address this risk in patients with HCT so that we can eventually improve outcomes of patients undergoing allogeneic stem cell transplantation for myelofibrosis."