Trastuzumab Deruxtecan in HER2-Positive Breast Cancer

Cortés J, Kim S, Chung W, et al. Trastuzumab deruxtecan versus trastuzumab emtansine for breast cancer. N Engl J Med. 2022;386:1143-1154. doi:10.1056/NEJMoa2115022

Modi S, Jacot W, Yamashita T, et al. Trastuzumab deruxtecan in previously treated HER2-low advanced breast cancer. N Engl J Med. 2022;387(1):9-22. doi:10.1056/NEJMoa2203690

Study 1 Overview (Cortés et al)

Objective: To compare the efficacy and safety of trastuzumab deruxtecan with those of trastuzumab emtansine in patients with HER2-positive metastatic breast cancer previously treated with trastuzumab and taxane.

Design: Phase 3, multicenter, open-label randomized trial conducted at 169 centers and 15 countries.

Setting and participants: Eligible patients had to have unresectable or metastatic HER2-positive breast cancer that had progressed during or after treatment with trastuzumab and a taxane or had disease that progressed within 6 months after neoadjuvant or adjuvant treatment involving trastuzumab or taxane. Patients with stable or previously treated brain metastases were eligible. Patients were not eligible for the study if they had symptomatic brain metastases, prior exposure to trastuzumab emtansine, or a history of interstitial lung disease.

Intervention: Patients were randomized in a 1-to-1 fashion to receive either trastuzumab deruxtecan 5.4 mg/kg every 3 weeks or trastuzumab emtansine 3.6 mg/kg every 3 weeks. Patients were stratified according to hormone-receptor status, prior treatment with epratuzumab, and the presence or absence of visceral disease.

Main outcome measures: The primary endpoint of the study was progression-free survival as determined by an independent central review. Secondary endpoints included overall survival, overall response, and safety.

Main results: A total of 524 patients were enrolled in the study, with 261 patients randomized to trastuzumab deruxtecan and 263 patients randomized to trastuzumab emtansine. The demographic and baseline characteristics were similar between the 2 cohorts, and 60% of patients in both groups received prior epratuzumab therapy. Stable brain metastases were present in around 20% of patients in each group, and 70% of patients in each group had visceral disease. The median duration of follow-up was 16.2 months with trastuzumab deruxtecan and 15.3 months with trastuzumab emtansine.

The median progression-free survival was not reached in the trastuzumab deruxtecan group and was 6.8 months in the trastuzumab emtansine group (95% CI, 5.6-8.2). At 12 months the percentage of patients alive without disease progression was significantly larger in the trastuzumab deruxtecan group compared with the trastuzumab emtan-

sine group. The hazard ratio for disease progression or death from any cause was 0.28 (95% CI, 0.22-0.37; $P < .001$). Subgroup analyses showed a benefit in progression-free survival with trastuzumab deruxtecan across all subgroups.

At the time of this analysis, the percentage of patients who were alive at 12 months was 94% with trastuzumab deruxtecan and 85.9% with trastuzumab emtansine. The response rates were significantly higher with trastuzumab deruxtecan compared with trastuzumab emtansine (79.7% vs 34.2%). A complete response was seen in 16% of patients in the trastuzumab deruxtecan arm, compared with 8.7% of patients in the trastuzumab emtansine group. The disease control rate (complete response, partial response, or stable disease) was higher in the trastuzumab deruxtecan group compared with the trastuzumab emtansine group (96.6% vs 76.8%).

Serious adverse events were reported in 19% of patients in the trastuzumab deruxtecan group and 18% of patients in the trastuzumab emtansine group. Discontinuation due to adverse events was higher in the trastuzumab deruxtecan group, with 13.6% of patients discontinuing trastuzumab deruxtecan. Grade 3 or higher adverse events were seen in 52% of patients treated with trastuzumab deruxtecan and 48% of patients treated with trastuzumab emtansine. The most commonly reported adverse event with trastuzumab deruxtecan was nausea/vomiting and fatigue. These adverse events were seen more in the trastuzumab deruxtecan group compared with the trastuzumab emtansine group. No drug-related grade 5 adverse events were reported.

In the trastuzumab deruxtecan group, 10.5% of patients receiving trastuzumab deruxtecan developed interstitial lung disease or pneumonitis. Seven patients had grade 1 events, 18 patients had grade 2 events, and 2 patients had grade 3 events. No grade 4 or 5 events were noted in either treatment group. The median time to onset of interstitial lung disease or pneumonitis in those receiving trastuzumab deruxtecan was 168 days (range, 33-507). Discontinuation of therapy due to interstitial lung disease or pneumonitis occurred in 8% of patients receiving trastuzumab deruxtecan and 1% of patients receiving trastuzumab emtansine.

Conclusion: Trastuzumab deruxtecan significantly decreases the risk of disease progression or death compared to trastuzumab emtansine in patients with HER2-positive metastatic breast cancer who have progressed on prior trastuzumab and taxane-based therapy.

Study 2 Overview (Modi et al)

Objective: To assess the efficacy of trastuzumab deruxtecan in patients with unresectable or metastatic breast cancer with low levels of HER2 expression.

Design: This was a randomized, 2-group, open-label, phase 3 trial.

Setting and participants: The trial was designed with a planned enrollment of 480 patients with hormone receptor–positive disease and 60 patients with hormone receptor–negative disease. Patients were randomized in a 2:1 ratio. Randomization was stratified according to HER2 status (immunohistochemical [IHC] 1+ vs IHC 2+/in situ hybridization [ISH] negative), number of prior lines of therapy, and hormone-receptor status. IHC scores for HER2 expression were determined through central testing. Specimens that had HER2 IHC scores of 2+ were reflexed to ISH. Specimens were considered HER2-low-expressing if they had an IHC score of 1+ or if they had an IHC score of 2+ and were ISH negative.

Eligible patients had to have received chemotherapy for metastatic disease or had disease recurrence during or within 6 months after completing adjuvant chemotherapy. Patients with hormone receptor–positive disease must have had at least 1 line of endocrine therapy. Patients were eligible if they had stable brain metastases. Patients with interstitial lung disease were excluded.

Intervention: Patients were randomized to receive trastuzumab deruxtecan 5.4 mg/kg every 3 weeks or physician's choice of chemotherapy (capecitabine, eribulin, gemcitabine, paclitaxel, or nab-paclitaxel).

Main outcome measures: The primary endpoint was progression-free survival in patients with hormone receptor–positive disease. Secondary endpoints were progression-free survival among all patients, overall survival in hormone receptor–positive patients, and overall survival in all patients. Additional secondary endpoints included objective response rates, duration of response, and efficacy in hormone receptor–negative patients.

Main results: A total of 373 patients were assigned to the trastuzumab deruxtecan group and 184 patients were

assigned to the physician's choice chemotherapy group; 88% of patients in each cohort were hormone receptor–positive. In the physician's choice chemotherapy group, 51% received eribulin, 20% received capecitabine, 10% received nab-paclitaxel, 10% received gemcitabine, and 8% received paclitaxel. The demographic and baseline characteristics were similar between both cohorts. The median duration of follow-up was 18.4 months.

The median progression-free survival in the hormone receptor–positive cohort was 10.1 months in the trastuzumab deruxtecan group and 5.4 months in the physician's choice chemotherapy group (HR, 0.51; 95% CI, 0.4-0.64). Subgroup analyses revealed a benefit across all subgroups. The median progression-free survival among patients with a HER2 IHC score of 1+ and those with a HER2 IHC score of 2+/negative ISH were identical. In patients who received a prior CDK 4/6 inhibitor, the median progression-free survival was also 10 months in the trastuzumab deruxtecan group. In those who were CDK 4/6- naïve, the progression-free survival was 11.7 months. The progression-free survival in all patients was 9.9 months in the trastuzumab deruxtecan group and 5.1 months in the physician's choice chemotherapy group (HR, 0.46; 95% CI, 0.24-0.89).

The median overall survival in the hormone receptor–positive cohort was 23.9 months in the trastuzumab deruxtecan group compared with 17.5 months in the physician's choice chemotherapy group (HR, 0.64; 95% CI, 0.48-0.86; $P = .003$). The median overall survival in the entire population was 23.4 months in the trastuzumab deruxtecan group vs 16.8 months in the physician's choice chemotherapy group. In the hormone receptor–negative cohort, the median overall survival was 18.2 months in the trastuzumab deruxtecan group and 8.3 months in the physician's choice chemotherapy group. Complete responses were seen in 3.6% in the trastuzumab deruxtecan group and 0.6% and the physician's choice chemotherapy group. The median duration of response was 10.7 months in the trastuzumab deruxtecan group and 6.8 months in the physician's choice chemotherapy group.

Incidence of serious adverse events was 27% in the trastuzumab deruxtecan group and 25% in the physician's choice chemotherapy group. Grade 3 or higher events occurred in 52% of the trastuzumab deruxtecan group and 67% of the physician's choice chemotherapy group. Discontinuation due to adverse events occurred in 16% in the trastuzumab deruxtecan group and 18% in the physician's choice chemotherapy group; 14 patients in the trastuzumab deruxtecan group and 5 patients in the physician's choice chemotherapy group had an adverse event that was associated with death. Death due to pneumonitis in the trastuzumab deruxtecan group occurred in 2 patients. Drug-related interstitial lung disease or pneumonitis occurred in 45 patients who received trastuzumab deruxtecan. The majority of these events were grade 1 and grade 2. However, 3 patients had grade 5 interstitial lung disease or pneumonitis.

Conclusion: Treatment with trastuzumab deruxtecan led to a significant improvement in progression-free survival compared to physician's choice chemotherapy in patients with HER2-low metastatic breast cancer.

Commentary

Trastuzumab deruxtecan is an antibody drug conjugate that consists of a humanized anti-HER2 monoclonal antibody linked to a topoisomerase 1 inhibitor. This antibody drug conjugate is unique compared with prior antibody drug conjugates such as trastuzumab emtansine in that it has a high drug-to-antibody ratio (~8). Furthermore, there appears to be a unique bystander effect resulting in off-target cytotoxicity to neighboring tumor cells, enhancing the efficacy of this novel therapy. Prior studies of trastuzumab deruxtecan have shown durable activity in heavily pretreated patients with metastatic HER2-positive breast cancer.[1]

HER2-positive breast cancer represents approximately 20% of breast cancer cases in women.[2] Historically, HER2 positivity has been defined by strong HER2 expression with IHC staining (ie, score 3+) or HER2 amplification through ISH. Conversely, HER2-negative disease has historically been defined as those with IHC scores of 0 or 1+. This group represents approximately 60% of HER2-negative metastatic breast cancer patients.[3] These patients have limited targeted treatment options after progressing on primary therapy. Prior data has shown that patients with low HER2 expression represent a heterogeneous population and thus, the historic categorization of HER2 status as positive or negative may in fact not adequately characterize the proportion of patients who

may derive clinical benefit from HER2-directed therapies. Nevertheless, there have been no data to date that have shown improved outcomes in low HER2 expressers with anti-HER2 therapies.

The current studies add to the rapidly growing body of literature outlining the efficacy of the novel antibody drug conjugate trastuzumab deruxtecan. The implications of the data presented in these 2 studies are immediately practice changing.

In the DESTINY-Breast03 trial, Cortéz and colleagues show that trastuzumab deruxtecan therapy significantly prolongs progression-free survival compared with trastuzumab emtansine in patients with HER2-positive metastatic breast cancer who have progressed on first-line trastuzumab and taxane-based therapy. With a hazard ratio of 0.28 for disease progression or death, the efficacy of trastuzumab deruxtecan highlighted in this trial clearly makes this the standard of care in the second-line setting for patients with metastatic HER2-positive breast cancer. The overall survival in this trial was immature at the time of this analysis, and thus continued follow-up to validate the results noted here are warranted.

The DESTINY-Breast04 trial by Modi et al expands the cohort of patients who benefit from trastuzumab deruxtecan profoundly. This study defines a population of patients with HER2-low metastatic breast cancer who will now be eligible for HER2-directed therapies. These data show that therapy with trastuzumab deruxtecan leads to a significant and clinically meaningful improvement in both progression-free survival and overall survival compared with chemotherapy in patients with metastatic breast cancer with low expression of HER2. This benefit was seen in both the estrogen receptor–positive cohort as well as the entire population, including pre-treated triple-negative disease. Furthermore, this study does not define a threshold of HER2 expression by IHC that predicts benefit with trastuzumab deruxtecan. Patients with an IHC score of 1+ as well as those with a score of 2+/ISH negative both benefit to a similar extent from trastuzumab deruxtecan. Interestingly, in the DAISY trial, antitumor activity was noted with trastuzumab deruxtecan even in those without any detectable HER2 expression on IHC.[4] Given the inconsistency and potential false negatives of IHC along with heterogeneous HER2 expression, further work is needed to better identify patients with low levels of HER2 expression who may benefit from this novel antibody drug conjugate. Thus, a reliable test to quantitatively assess the level of HER2 expression is needed in order to determine more accurately which patients will benefit from trastuzumab deruxtecan.

Last, trastuzumab deruxtecan has been associated with interstitial lung disease and pneumonitis. Interstitial lung disease and pneumonitis occurred in approximately 10% of patients who received trastuzumab deruxtecan in the DESTINY-Breast03 trial and about 12% of patients in the DESTINY-Breast04 trial. Most of these events were grade 1 and grade 2. Nevertheless, clinicians must be aware of this risk and monitor patients frequently for the development of pneumonitis or interstitial lung disease.

Application for Clinical Practice and System Implementation

The results of the current studies show a longer progression-free survival with trastuzumab deruxtecan in both HER2-low expressing metastatic breast cancer and HER2-positive metastatic breast cancer following taxane and trastuzumab-based therapy. These results are clearly practice changing and represent a new standard of care in these patient populations. It is incumbent upon treating oncologists to work with our pathology colleagues to assess HER2 IHC thoroughly in order to identify all potential patients who may benefit from trastuzumab deruxtecan in the metastatic setting. The continued advancement of anti-HER2 therapy will undoubtedly have a significant impact on patient outcomes going forward.

Practice Points

- With a hazard ratio of 0.28 for disease progression or death, the efficacy of trastuzumab deruxtecan highlighted in the DESTINY-Breast03 trial clearly makes this the standard of care in the second-line setting for patients with metastatic HER2-positive breast cancer.
- In the DESTINY-Breast04 trial, a significant and clinically meaningful improvement in both progression-free survival and overall survival compared with chemotherapy was seen in patients with metastatic breast cancer with low expression of HER2, including both the estrogen receptor–positive cohort as well as the

entire population, including those with pre-treated triple-negative disease.

References

1. Modi S, Saura C, Yamashita T, et al. Trastuzumab deruxtecan in previously treated HER2-positive breast cancer. *N Engl J Med.* 2020;382(7):610-621. doi:10.1056/NEJMoa1914510
2. National Cancer Institute. Cancer stat facts. female breast cancer. Accessed July 25, 2022. https://seer.cancer.gov/statfacts/html/breast.html
3. Schettini F, Chic N, Braso-Maristany F, et al. Clinical, pathological and PAM50 gene expression features of HER2-low breast cancer. *NPJ Breast Cancer.* 2021;7(1):1. doi:10.1038/s41523-020-00208-2
4. Dieras VDE, Deluche E, Lusque A, et al. Trastuzumab deruxtecan for advanced breast cancer patients, regardless of HER2 status: a phase II study with biomarkers analysis. In: *Proceedings of Abstracts of the 2021 San Antonio Breast Cancer Symposium*, December 7-10, 2021. San Antonio: American Association for Cancer Research, 2021. Abstract.

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Geriatric-Centered Interdisciplinary Care Pathway Reduces Delirium in Hospitalized Older Adults With Traumatic Injury

Park C, Bharija A, Mesias M, et al. Association between implementation of a geriatric trauma clinical pathway and changes in rates of delirium in older adults with traumatic injury. JAMA Surg. 2022 Jun 8;e221556. doi:10.1001/jamasurg.2022.1556

Bryant EA, Tulebaev S, Castillo-Angeles M, et al. Frailty identification and care pathway: an interdisciplinary approach to care for older trauma patients. J Am Coll Surg. 2019;228(6):852-859.e1. doi:10.1016/j.jamcollsurg.2019.02.052

Study 1 Overview (Park et al)

Objective: To examine whether implementation of a geriatric trauma clinical pathway is associated with reduced rates of delirium in older adults with traumatic injury.

Design: Retrospective case-control study of electronic health records.

Setting and participants: Eligible patients were persons aged 65 years or older who were admitted to the trauma service and did not undergo an operation. A Geriatric Trauma Care Pathway was developed by a multidisciplinary Stanford Quality Pathways team and formally launched on November 1, 2018. The clinical pathway was designed to incorporate geriatric best practices, which included order sets (eg, age-appropriate nonpharmacological interventions and pharmacological dosages), guidelines (eg, Institute for Healthcare Improvement Age-Friendly Health systems 4M framework), automated consultations (comprehensive geriatric assessment), and escalation pathways executed by a multidisciplinary team (eg, pain, bowel, and sleep regulation). The clinical pathway began with admission to the emergency department (ED) (ie, automatic trigger of geriatric trauma care admission order set), daily multidisciplinary team meetings during acute hospitalization, and a transitional care team consultation for postdischarge follow-up or home visit.

Main outcome measures: The primary outcome was delirium as determined by a positive Confusion Assessment Method (CAM) score or a diagnosis of delirium by the clinical team. The secondary outcome was hospital length of stay (LOS). Process measures for pathway compliance (eg, achieving adequate pain control, early mobilization, advance care planning) were assessed. Outcome measures were compared between patients who underwent the Geriatric Trauma Care Pathway intervention (postimplementation

group) vs patients who were treated prior to pathway implementation (baseline pre-implementation group).

Main results: Of the 859 eligible patients, 712 were included in the analysis (442 [62.1%] in the baseline pre-implementation group and 270 [37.9%] in the postimplementation group); mean (SD) age was 81.4 (9.1) years, and 394 (55.3%) were women. The injury mechanism was similar between groups, with falls being the most common cause of injury (247 [55.9%] in the baseline group vs 162 [60.0%] in the postimplementation group; $P = .43$). Injuries as measured by Injury Severity Score (ISS) were minor or moderate in both groups (261 [59.0%] in baseline group vs 168 [62.2%] in postimplementation group; $P = .87$). The adjusted odds ratio (OR) for delirium in the postimplementation group was lower compared to the baseline pre-implementation group (OR, 0.54; 95% CI, 0.37-0.80; $P < .001$). Measures of advance care planning in the postimplementation group improved, including more frequent goals-of-care documentation (53.7% in postimplementation group vs 16.7% in baseline group; $P < .001$) and a shortened time to first goals-of-care discussion upon presenting to the ED (36 hours in postimplementation group vs 50 hours in baseline group; $P = .03$).

Conclusion: Implementation of a multidisciplinary geriatric trauma clinical pathway for older adults with traumatic injury at a single level I trauma center was associated with reduced rates of delirium.

Study 2 Overview (Bryant et al)

Objective: To determine whether an interdisciplinary care pathway for frail trauma patients can improve in-hospital mortality, complications, and 30-day readmissions.

Design: Retrospective cohort study of frail patients.

Setting and participants: Eligible patients were persons aged 65 years or older who were admitted to the trauma service and survived more than 24 hours; admitted to and discharged from the trauma unit; and determined to be pre-frail or frail by a geriatrician's assessment. A Frailty Identification and Care Pathway designed to reduce delirium and complications in frail older trauma patients was developed by a multidisciplinary team and implemented in 2016. The standardized evidence-based interdisciplinary care pathway included utilization of order sets and interventions for delirium prevention, early ambulation, bowel and pain regimens, nutrition and physical therapy consults, medication management, care-goal setting, and geriatric assessments.

Main outcome measures: The main outcomes were delirium as determined by a positive CAM score, major complications as defined by the Trauma Quality Improvement Project, in-hospital mortality, and 30-day hospital readmission. Outcome measures were compared between patients who underwent Frailty Identification and Care Pathway intervention (postintervention group) vs patients who were treated prior to pathway implementation (pre-intervention group).

Main results: A total of 269 frail patients were included in the analysis (125 in pre-intervention group vs 144 in postintervention group). Patient demographic and admission characteristics were similar between the 2 groups: mean age was 83.5 (7.1) years, 60.6% were women, and median ISS was 10 (interquartile range [IQR], 9-14). The injury mechanism was similar between groups, with falls accounting for 92.8% and 86.1% of injuries in the pre-intervention and postintervention groups, respectively ($P = .07$). In univariate analysis, the Frailty Identification and Care Pathway intervention was associated with a significant reduction in delirium (12.5% vs 21.6%, $P = .04$) and 30-day hospital readmission (2.7% vs 9.6%, $P = .01$) compared to patients in the pre-intervention group. However, rates of major complications (28.5% vs 28.0%, $P = 0.93$) and in-hospital mortality (4.2% vs 7.2%, $P = .28$) were similar between the pre-intervention and postintervention groups. In multivariate logistic regression models adjusted for patient characteristics (age, sex, race, ISS), patients in the postintervention group had lower delirium (OR, 0.44; 95% CI, 0.22-0.88; $P = .02$) and 30-day hospital readmission (OR, 0.25; 95% CI, 0.07-0.84; $P = .02$) rates compared to those in the pre-intervention group.

Conclusion: Implementation of an interdisciplinary care protocol for frail geriatric trauma patients significantly decreased their risks for in-hospital delirium and 30-day hospital readmission.

Commentary

Traumatic injuries in older adults are associated with higher morbidity and mortality compared to younger patients, with falls and motor vehicle accidents accounting for a

majority of these injuries. Astoundingly, up to one-third of this vulnerable population presenting to hospitals with an ISS greater than 15 may die during hospitalization.[1] As a result, a large number of studies and clinical trials have focused on interventions that are designed to reduce fall risks, and hence reduce adverse consequences of traumatic injuries that may arise after falls.[2] However, this emphasis on falls prevention has overshadowed a need to develop effective geriatric-centered clinical interventions that aim to improve outcomes in older adults who present to hospitals with traumatic injuries. Furthermore, frailty—a geriatric syndrome indicative of an increased state of vulnerability and predictive of adverse outcomes such as delirium—is highly prevalent in older patients with traumatic injury.[3] Thus, there is an urgent need to develop novel, hospital-based, traumatic injury–targeting strategies that incorporate a thoughtful redesign of the care framework that includes evidence-based interventions for geriatric syndromes such as delirium and frailty.

The study reported by Park et al (Study 1) represents the latest effort to evaluate inpatient management strategies designed to improve outcomes in hospitalized older adults who have sustained traumatic injury. Through the implementation of a novel multidisciplinary Geriatric Trauma Care Pathway that incorporates geriatric best practices, this intervention was found to be associated with a 46% lower risk of in-hospital delirium. Because of the inclusion of all age-eligible patients across all strata of traumatic injuries, rather than preselecting for those at the highest risk for poor clinical outcomes, the benefits of this intervention extend to those with minor or moderate injury severity. Furthermore, the improvement in delirium (ie, the primary outcome) is particularly meaningful given that delirium is one of the most common hospital-associated complications that increase hospital LOS, discharge to an institution, and mortality in older adults. Finally, the study's observed reduced time to a first goals-of-care discussion and increased frequency of goals-of-care documentation after intervention should not be overlooked. The improvements in these 2 process measures are highly significant given that advanced care planning, an intervention that helps to align patients' values, goals, and treatments, is completed at substantially lower rates in older adults in the acute hospital setting.[4]

Similarly, in an earlier published study, Bryant and colleagues (Study 2) also show that a geriatric-focused interdisciplinary trauma care pathway is associated with delirium risk reduction in hospitalized older trauma patients. Much like Study 1, the Frailty Identification and Care Pathway utilized in Study 2 is an evidence-based interdisciplinary care pathway that includes the use of geriatric assessments, order sets, and geriatric best practices. Moreover, its exclusive inclusion of pre-frail and frail older patients (ie, those at higher risk for poor outcomes) with moderate injury severity (median ISS of 10 [IQR, 9-14]) suggests that this type of care pathway benefits hospitalized older trauma patients, who are particularly vulnerable to adverse complications such as delirium. Moreover, the successful utilization of the FRAIL questionnaire, a validated frailty screening tool, by surgical residents in the ED to initiate this care pathway demonstrates the feasibility of its use in expediting frailty screening in older patients in trauma care.

Application for Clinical Practice and System Implementation

Findings from the 2 studies discussed in this review indicate that implementation of interdisciplinary clinical care pathways predicated on evidence-based geriatric principles and best practices is a promising approach to reduce delirium in hospitalized older trauma patients. These studies have helped to lay the groundwork in outlining the roadmaps (eg, processes and infrastructures) needed to create such clinical pathways. These key elements include: (1) integration of a multidisciplinary committee (eg, representation from trauma, emergency, and geriatric medicine, nursing, physical and occupational therapy, pharmacy, social work) in pathway design and implementation; (2) adaption of evidence-based geriatric best practices (eg, the Institute for Healthcare Improvement Age-Friendly Health System 4M framework [medication, mentation, mobility, what matters]) to prioritize interventions and to design a pathway that incorporates these features; (3) incorporation of comprehensive geriatric assessment by interdisciplinary providers; (4) utilization of validated clinical instruments to assess physical and cognitive functions, frailty, delirium, and social determinants of health; (5) modification of electronic health record systems to encompass order sets that incorporate

evidence-based, nonpharmacological and pharmacological interventions to manage symptoms (eg, delirium, pain, bowel movement, sleep, immobility, polypharmacy) essential to quality geriatric care; and (6) integration of patient and caregiver preferences via goals-of-care discussions and corresponding documentation and communication of these goals.

Additionally, these 2 studies imparted some strategies that may facilitate the implementation of interdisciplinary clinical care pathways in trauma care. Examples of such facilitators include: (1) collaboration with champions within each specialty to reinforce education and buy-in; (2) creation of automatically triggered order sets upon patient presentation to the ED that unites distinct features of clinical pathways; (3) adaption and reorganization of existing hospital infrastructures and resources to meet the needs of clinical pathways implementation (eg, utilizing information technology resources to develop electronic health record order sets; using quality department to develop clinical pathway guidelines and electronic outcome dashboards); and (4) development of individualized patient and caregiver education materials based on care needs (eg, principles of delirium prevention and preservation of mobility during hospitalization) to prepare and engage these stakeholders in patient care and recovery.

Practice Points

- A geriatric interdisciplinary care model can be effectively applied to the management of acute trauma in older patients.
- Interdisciplinary clinical pathways should incorporate geriatric best practices and guidelines and age-appropriate order sets to prioritize and integrate care.

References

1. Hashmi A, Ibrahim-Zada I, Rhee P, et al. Predictors of mortality in geriatric trauma patients: a systematic review and meta-analysis. *J Trauma Acute Care Surg.* 2014;76(3):894-901. doi:10.1097/TA.0b013e3182ab0763
2. Hopewell S, Adedire O, Copsey BJ, et al. Multifactorial and multiple component interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev.* 2018;7(7):CD012221. doi:10.1002/14651858.CD012221.pub2
3. Joseph B, Pandit V, Zangbar B, et al. Superiority of frailty over age in predicting outcomes among geriatric trauma patients: a prospective analysis. *JAMA Surg.* 2014;149(8):766-772. doi:10.1001/jamasurg.2014.296
4. Hopkins SA, Bentley A, Phillips V, Barclay S. Advance care plans and hospitalized frail older adults: a systematic review. *BMJ Support Palliat Care.* 2020;10(2):164-174. doi:10.1136/bmjspcare-2019-002093

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