Years of Life Lost After Complications of Coronary Artery Bypass Operations

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Background. **We currently have an incomplete understanding of which postoperative complications after coronary artery bypass grafting (CABG) are associated with long-term death. The purpose of this study was to find the associations between complications and attributable death.**

Methods. **Prospectively collected data on patient characteristics, risk factors, and complications of patients undergoing isolated CABG with 20-year follow-up were analyzed with a Cox regression model to calculate the overall hazard of dying associated with each postoperative complication. An individual's age and hazard of dying from each complication were then used to calculate years of life lost to each complication.**

Results. **The postoperative mortality rate was 0.79% (69 of 8,773) at 30 days, 2.85% (250 of 8,773) at 180 days, and 6.38% (560 of 8,773) at 2 years. At a median follow-up of 9.8 years, 1,891 patients (21.6%) had died. Postoperative complications occurred in 3,438 patients (39.2%). Cardiac arrest (hazard ratio, 2.153), reoperation (hazard ratio, 1.679), and new dialysis (hazard ratio, 1.64) were the complications with the greatest hazard of death. After adjusting for complication incidence and patient age, cardiac arrest (703 years), reoperation (544 years), atrial fibrillation (470 years), and prolonged mechanical ventilation (371 years) were associated with the greatest number of years of life lost.**

Conclusions. **Acute cardiac arrest, reoperation for other cardiac reasons, new dialysis, atrial fibrillation, and prolonged mechanical ventilation are associated with the largest increase in attributable deaths. Prevention and treatment of these complications may improve mortality rates after cardiac operations.**

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The Society of Thoracic Surgeons Quality Measurement Task Force chose death after coronary artery bypass graft (CABG) operations as a key national benchmark for comparison of perioperative care [1–3]. The operative mortality rate (defined as death during index admission or out-of-hospital death within 30 days) after CABG is 1% to 3% [2, 4, 5]. The annual mortality rate after CABG operations ranges from 2.7% to 4.2% [6–8], which leads to 9% to 10.2%, 26.4%, and 64.4% of patients having died at 5, 10, and 20 years, respectively [6, 9, 10].

A problem with using just the operative mortality rate as the quality benchmark is that it does not account for deaths that occur more than 30 days after discharge or provide insight into the cause of death. Complications will occur in half of patients undergoing cardiac operations, and although most—particularly the most common complications—rarely lead to death during the same hospitalization, they may be associated with increased late death [11]. Consequently, such complications, especially if common (eg, postoperative atrial fibrillation), may have a large effect on the total years of life lost. Such attributable loss of life may be more significant for younger patients. Therefore, the long-term effect of various postoperative complications must be understood to optimally guide future improvement efforts. Because complications may be preventable (or more optimally treated), complications associated with more years of life lost may be prime candidates for deployment of targeted efforts.

Our study tested the hypothesis that the years of life lost attributable to different postoperative complications will vary considerably. Consequently, attributable death and years of life lost may be reduced by targeting care improvement and complication reduction efforts toward those complications with the largest effects on late death.

Patients and Methods

Institutional Review Board approval and waiver of informed consent was obtained for this project from

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Mercy St. Vincent Medical Center, Toledo, Ohio, and from the University of Michigan, Ann Arbor, Michigan (HUM00108370). This study is a retrospective analysis of existing registry data derived from the institutional cardiac surgery database from a large, tertiary care hospital in Northwest Ohio. All CABG operations performed in adults (≥18 years) at the hospital were eligible for inclusion in this study.

Data Collection

Trained reviewers were responsible for collecting and verifying data, including the presence of complications and date of patient death. Data definitions used were those in effect in The Society of Thoracic Surgeons database at the time of data collection [1, 12, 13]. The Society of Thoracic Surgeons database defines a complication as a postoperative event that occurs during the index hospitalization for the operation, including the entire perioperative period, even if it occurs more than 30-days postoperatively.

Death data were obtained from a combination of hospital and physician medical records, the Social Security Death Index (through December 18, 2011, when its availability was restricted by governmental regulations due to privacy concerns [14] and death data from the state of Ohio through December 31, 2013. Patients with a home address documented as being in a state other than Ohio were censored from analysis after December 18, 2011, because of unavailability of death records.

Statistical Analysis

Univariate descriptive analyses were performed on all independent variables in the database, including 32 postoperative complications, patient comorbidities, and procedural factors. Comparisons between groups were made using the Student, Mann-Whitney-Wilcoxon, Pearson χ^2, and Fisher exact tests, as appropriate. Unadjusted mortality rates were calculated for each complication.

To adjust for patient demographics, comorbidities and procedural factors, a semiparsimonious multivariate Cox regression model was fit using the variables in Table 1 and 17 of the postoperative complications for four distinct postoperative periods: less than 30 days, 31 to 180 days, 181 days to 2 years, and more than 2 years. The same regression was performed for overall deaths. Complications with fewer than 40 total occurrences were excluded, as was postoperative pneumonia because of collinearity with prolonged mechanical ventilation, and the variable denoting that an unlisted complication had occurred. Stroke, transient ischemic attack, and coma were combined into a composite neurologic complication. Akaike information criterion was used to select models in a stepwise fashion based on the maximum value of the likelihood function. This minimizes information loss in model selection and makes hypothesis testing superfluous [15–17].

An adjusted hazard ratio (HR) was estimated for each complication remaining after variable selection. Cox regression estimates were used to calculate separate survival curves for each complication and one for patients with no complications. The area between the curve describing no complications and each complication's survival curve, adjusted for other complications, was thus the years of life lost per patient with that complication [18]. This was then multiplied by the number of patients with that complication to estimate the number of years lost in the entire population over the follow-up time ("population years of life lost"). The 95% confidence intervals (CIs) were estimated using a nonparametric bootstrap of the population. All data processing and statistical analyses were completed using SPSS 22 software (IBM Corp, Armonk, NY) and R 3.2.2 software (R Foundation for Statistical Computing, Vienna, Austria).

Table 1. Patient Factors

Attribute	No.	Mean	SD
Age, y	8,776	65	11
Weight, kg	8,775	86.9	18.6
Height, cm	8,776	171	10
Body surface area, m^2	8,775	2.0	0.2
Body mass index, kg/m^2	8,775	29.6	5.7
Perfusion time,[a] min	7,983	95	45
Cross-clamp time,[a] min	7,920	59	32
	No.	**Yes**	**%**
Female	8,776	2,786	32
Current smoker	8,776	172	2
History of			
Diabetes	8,776	3,240	37
Stroke	8,776	721	8
Peripheral vascular disease	8,776	1,556	18
Cerebrovascular disease	8,776	2,293	26
Congestive heart failure	8,776	1,305	15
Stable angina	8,776	4,320	49
Unstable angina	8,776	2,397	27
Preoperative medication use			
β-Blocker	8,775	5,921	68
Anticoagulation	8,775	3,547	40
Steroid	8,773	237	3
Aspirin	8,773	6,390	73
Any intraoperative blood product	8,776	3,383	39
COPD	8,776	1,888	22

[a] The operations in the remaining patients were done off pump or without an aortic cross-clamp.

COPD = chronic obstructive pulmonary disease.

Results

The study population consisted of 8,776 patients (68.2% men). Three patients were excluded from analysis, given missing data. Patients were an average age of 65 (SD, 11) years. Median postoperative length of stay was 6 days (interquartile range, 4 to 8 days; Table 1). The postoperative mortality rate was 0.79% (69 of 8,773) at 30 days, 2.85% (250 of 8,773) at 180 days, and 6.38% (560 of 8,773) at

Table 2. Complications Occurring in More Than 1% of Patients

Complication	No.	%
Any complication	3,438	39
New-onset atrial fibrillation or flutter	1,909	22
Prolonged mechanical ventilation (>24 hours)	945	11
Renal failure	463	5
Gastrointestinal complication	286	3
Reoperation for mediastinal bleeding or tamponade	273	3
Reoperation for noncardiac reasons	268	3
Pneumonia	231	3
Myocardial infarction ≤24 hours postoperatively	219	3
Cardiac arrest	196	2
Reoperation for other cardiac reasons	187	2
Multisystem organ dysfunction	137	2
Stroke with deficit	133	2

2 years. Late mortality was 21.6% (1,891 of 8,773) at a median follow-up of 9.8 years.

Postoperative complications occurred in 3,438 patients (39.2%). The most common complications were atrial fibrillation (21.8%), prolonged mechanical ventilation (10.8%), and renal failure (5.3%; Table 2). The complications associated with the highest univariate risk of overall death were new need for dialysis (HR, 6.02; 95% CI, 4.17 to 8.69; $p < 0.001$), cardiac arrest (HR, 5.43; 95% CI, 4.60 to 6.41; $p < 0.001$), multisystem organ dysfunction (HR, 5.35; 95% CI, 4.38 to 6.54; $p < 0.001$), and reoperation for other cardiac reasons (HR, 2.86; 95% CI, 2.37 to 3.45; $p < 0.001$).

After adjusting for patient factors and the other complications that occurred, cardiac arrest (HR, 2.15; 95% CI, 1.76 to 2.64; $p < 0.001$), reoperation for other cardiac reasons (HR, 1.68; 95% CI, 1.38 to 2.04; $p < 0.001$), and new need for dialysis (HR, 1.64; 95% CI, 1.09 to 2.46; $p = 0.017$) were associated with the highest adjusted hazard of overall death (Table 3). Atrial fibrillation was the most common complication, but it had a low adjusted risk of death (HR, 1.06; 95% CI, 0.98 to 1.16; $p = 0.148$; Fig 1).

The association between death and complications varied by time period (Table 4). Certain complications, notably cardiac arrest and reoperation for noncardiac reasons, were associated with both early and late death. Cardiac tamponade, new need for dialysis, and prolonged mechanical ventilation were only associated with early death.

Four complications were associated with greater than 1 year of life lost (per patient, per the 20-year follow-up period): acute cardiac arrest (3.59 years; 95% CI, 2.10 to 5.54 years), reoperation for other cardiac reasons (2.32 years; 95% CI, 0.93 to 3.51 years), new need for dialysis (2.20 years; 95% CI, –0.93 to 6.18 years), and multisystem organ dysfunction (1.84 years; 95% CI, 0.06 to 3.86 years). Another five were associated with less than 1 year of life lost (per patient, per the 20-year follow-up; Fig 2 and Table 3).

Table 3. Adjusted Hazard of Death and Adjusted Years of Life Lost After Complication, per 20 Years[a]

	Hazard of Death				Years of Life Lost per 20 Years					
Postoperative Complication	Hazard Ratio	Lower 95% CI	Upper 95% CI	p Value	Per Patient	Lower 95% CI	Upper 95% CI	Per Population of 8,773 Patients	Lower 95% CI	Upper 95% CI
Cardiac arrest	2.153	1.757	2.638	<0.001	3.59	2.10	5.54	703	390	1,130
Reoperation for other cardiac reasons	1.679	1.379	2.045	<0.001	2.32	0.93	3.51	544	173	647
New need for dialysis	1.640	1.094	2.459	0.017	2.20	–0.93	6.18	97	–37	264
Multisystem organ dysfunction	1.523	1.183	1.959	0.001	1.84	0.06	3.86	252	8	530
Reoperation for noncardiac reasons	1.171	0.974	1.409	0.093	0.65	–0.26	1.69	174	–70	453
Gastrointestinal complication	1.142	0.953	1.370	0.150	0.54	–0.47	1.43	155	–138	432
Renal failure	1.116	0.964	1.294	0.143	0.45	–0.27	1.24	206	–126	588
Prolonged mechanical ventilation (>24 hours)	1.102	0.972	1.250	0.129	0.39	–0.20	0.97	371	–186	922
New-onset atrial fibrillation or flutter	1.063	0.978	1.156	0.148	0.25	–0.13	0.59	470	–248	1,132

[a] The 95% CIs were calculated by a bootstrap (n = 500). The population size = 8,773 patients.

CI = confidence interval.

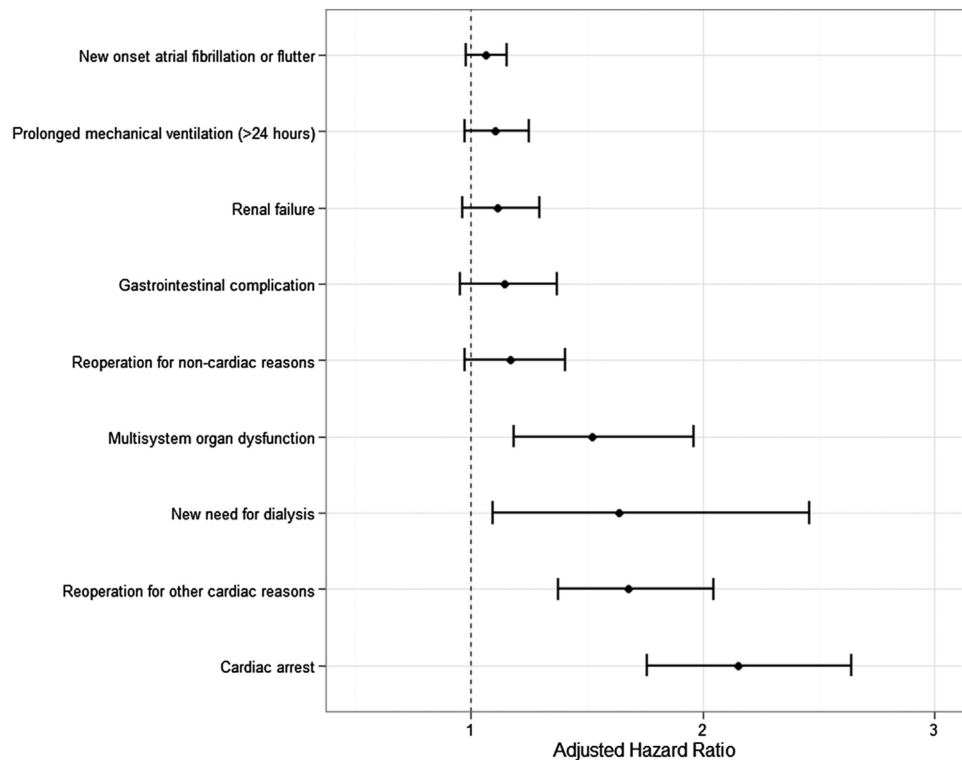

Fig 1. Forest plot of adjusted hazard ratio (squares) of death for complications with the 95% confidence interval (horizontal lines).

After adjusting for patient factors and the incidence of each complication, we found that cardiac arrest was associated with the most years of life lost: 703 years (95% CI, 390 to 1,130 years; 80.1 years of life lost per 1,000 patients and 20-year follow-up). The effects persisted even when the patients survived the cardiac arrest, and they experienced an elevated risk of death throughout all the time periods studied (Fig 2). New need for dialysis had a high number of years of life lost per occurrence, but because of its low overall incidence, had a relatively small number of years of life lost in the population: 97 years (95% CI, –37 to 264 years; 11.1 years of life lost per 1,000 patients and 20-year follow-up). Conversely, new-onset atrial fibrillation or flutter and prolonged mechanical ventilation both had a small average effect per occurrence but were associated with a large number of years of life lost in the population, reflecting their high incidence of 470 years (95% CI, –248 to 1,132 years; 53.6 years of life lost per 1,000 patients and 20-year follow-up) and 371 years (95% CI, –186 to 922; 42.3 years of life lost per 1,000 patients and 20-year follow-up), respectively (Table 3).

Comment

We found that the attributable mortality rate from complications after CABG was 339 deaths per 1,000 patients and the 20-year follow-up period, with cardiac arrest contributing the largest component (80.1 years of life lost per 1,000 patients per 20-year follow-up). Years of life lost is a combination of the HR and the frequency of the complication. Reoperation for other cardiac and noncardiac reasons had a similar rate of occurrence (Table 2), but reoperation for other cardiac reasons had a greater HR and, hence, a tripling of the years of life lost (Table 3).

Other studies have shown that these complications are associated with an increase in operative deaths and other short-term measures of death, but most have treated these complications in isolation and even fewer have studied long-term outcomes. Similar to other studies, we found that cardiac arrest, need for reoperation in the postoperative period, new need for dialysis, and multisystem organ dysfunction were associated with increased death [19–26]. However, our study expands on this knowledge by showing the relative contributions of different complications to years of life lost and adjusts for the fact that patients can have multiple complications but only one death. Also, examining the amount of life lost due to a complication adjusts for patient age. A death in a 35-year-old person contributes more than in a 90-year-old person because of the greater life expectancy of the younger person. Our models took this into account and adjusted not only for age but also for sex and race, which have differential effects on life expectancy.

Another strength of our findings is that by adjusting for other complications when calculating years of life lost, we can isolate the association of each particular complication to death, and by adjusting for patient characteristics and comorbidities, we can eliminate these effects on death. However, because this is a retrospective study, we cannot demonstrate causality, which would require a prospective interventional study.

Table 4. Hazard Ratio of Death by Postoperative Date and Complication[a]

	Time From the Operation															
	0–30 Days				31–180 Days				181 Days-2 Years				>2 Years			
Postoperative Complication	Hazard Ratio	Lower 95% CI	Upper 95% CI	*p* Value	Hazard Ratio	Lower 95% CI	Upper 95% CI	*p* Value	Hazard Ratio	Lower 95% CI	Upper 95% CI	*p* Value	Hazard Ratio	Lower 95% CI	Upper 95% CI	*p* Value
Cardiac arrest	8.14	4.33	15.31	<0.001	3.03	1.97	4.66	<0.001	3.05	1.95	4.77	<0.001	1.42	1.05	1.92	0.02
Cardiac tamponade	5.67	1.32	24.28	0.02												
Gastrointestinal complications									1.90	1.25	2.90	<0.001				
Leg vein harvest site infection													1.42	1.01	1.99	0.04
Multisystem organ dysfunction					2.64	1.63	4.28	<0.001	1.76	1.00	3.09	0.05				
New need for dialysis					2.67	1.39	5.12	<0.001								
Postoperative atrial fibrillation													1.09	0.99	1.20	0.07
Prolonged mechanical ventilation	3.32	1.79	6.16	<0.001	1.67	1.08	2.57	0.02								
Renal failure	1.84	0.95	3.57	0.07									1.22	1.04	1.44	0.02
Reoperation for																
Bleeding complications					1.56	0.97	2.53	0.07								
Noncardiac reasons					1.78	1.14	2.78	0.01	1.55	0.92	2.63	0.10	1.19	0.96	1.49	0.12
Other cardiac reasons					2.95	1.87	4.65	<0.001					1.37	1.06	1.79	0.02

[a] A blank cell indicates the postoperative complication was not associated with an increased hazard of dying in that time interval.

CI = confidence interval.

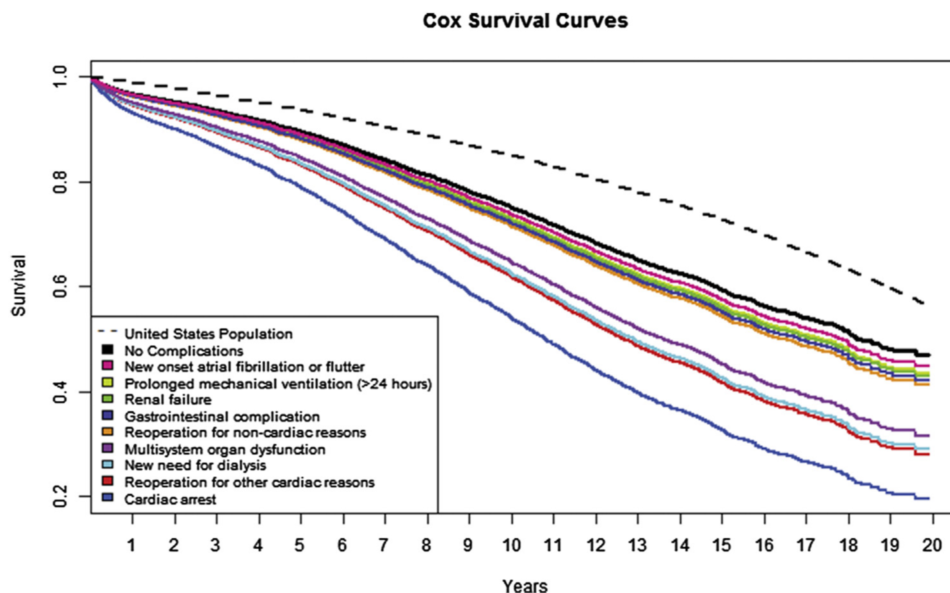

Fig 2. Cox survival curve comparing 20-year survival by complication for the United States population identically matched to the coronary artery bypass grafting (CABG) patients on the basis of age, sex, race, ethnicity (dotted line), patients who underwent CABG but did not experience a complication (black line), and patients who experienced selected postoperative complications (colored lines).

Some of the complications, such as reoperation for noncardiac reasons and prolonged mechanical ventilation, are themselves markers of a preexisting debilitated state or the occurrence of debility during their postoperative state that led to the need for an operation for noncardiac reasons (such as insertion of a gastrostomy feeding tube) or the need for prolonged mechanical ventilation. Engoren and colleagues [27] previously found that even small amounts of debility, such as not being able to adequately eat or to walk several feet, are associated with late death in patients with very prolonged mechanical ventilation after a cardiac operation. Further study is needed to find the underlying causes that contribute to these intermediate outcomes or processes of care and to late death.

The concept of years of life lost allows us to recognize which complications, if reduced, will provide the "biggest bang for the buck" for our patients and allow us to focus valuable time and limited resources on the complications with the highest effect. For example, a complication that is invariably fatal, but occurs rarely, may have a much smaller number of population years of life lost than a common complication that has lower fatality rate. Similarly, a death that occurs in a younger patient or soon after a complication will cause more years of life lost than another complication that causes death in older patients or years after it occurs. Calculating years of life lost associated with complications corrects for this. Despite its widespread adoption in other fields, this approach has not yet been widely adopted in cardiac surgery.

This study has several limitations. Although we excluded patients from states other than Ohio, death data may have been absent on some patients if they moved out of state and died after December 2011, after which time the Social Security Death Index data were not available and they would not have been present in the Ohio death list. This represents only 2 years of data and probably very few patients and is thus unlikely to present a significant bias. Second, because this is a single-center study, the results may not be generalizable to other centers or populations.

The wide CIs that were noted in some factors, such as atrial fibrillation, may be evidence for subpopulations within the complication. For example, atrial fibrillation may consist of several subpopulations: patients who quickly convert back to sinus rhythm and those who remain in atrial fibrillation long-term, further divided into those with and without complications of the disease or therapy. Further study is needed to better elucidate these subpopulations.

Certain strengths of the study deserve additional mention. This was a large study from a tertiary care hospital in the Upper Midwestern United States with a diverse patient population. Data were prospectively collected by trained individuals using consistent data definitions for comorbidities and complications. The database has the advantage of including all CABG cases performed at the institution, thereby eliminating the sampling bias inherent in other databases [22]. Subgroup analyses were conducted for death in four clinically relevant periods.

The use of the Akaike information criterion is another strength of the study. Unlike traditional p value–based statistical significance testing, the Akaike information criterion is based on the log likelihood and takes the number of factors analyzed into account when generating a model. This minimizes information loss in model selection and may retain important variables that may not be traditionally considered statistically significant [15–17, 28].

Assigning priority for allocation of scarce resources to prevent deaths after cardiac operations is difficult, particularly given the difficulties in determining whether complications are causally associated with death or are

merely epiphenomena that are markers of sicker patients who are more likely to die and not causally associated with subsequent death. Our data concerning the years of life lost per population, which reflect incidence, may be more likely to drive policy. Hospital administrators and policy experts will need to account for the lifetime cost of these complications in future studies to better account for their effect. Additional research is necessary to better understand how certain complications lead to increased early and late-term death. Furthermore, we did not assess quality adjusted life-years, which are an important patient-centered metric; future work will need to better evaluate this metric.

Although we monitored patients for as long as 20 years, future studies will ideally include even longer follow-up to better estimate the potential years of life lost after complications. Finally, multicenter efforts, with even larger sample sizes, could improve our estimates of years of life lost as a result of various postoperative complications. An improved understanding of these underlying mechanisms can improve prevention and treatment of postoperative complications and an improvement in postoperative mortality rates. These findings will also help clinicians understand the implications of complications if they occur to patients and help guide discussions with the patient and family members.

In conclusion, we found that acute cardiac arrest, reoperation for other cardiac reasons, new need for dialysis, prolonged mechanical ventilation, atrial fibrillation, and multisystem organ dysfunction are associated with the greatest number of years of life lost after CABG operations.

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