Pediatric Cardiovascular Morbidity of the Early Term Newborn

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Objective To determine whether early term delivery (at $37^{0/7}$-$38^{6/7}$ weeks of gestation) is associated with long-term pediatric cardiovascular morbidity of the offspring.

Study design A population-based cohort analysis was performed including all term deliveries occurring between 1991 and 2014 at a single tertiary medical center. Gestational age at delivery was subdivided into early term ($37^{0/7}$-$38^{6/7}$), full term ($39^{0/7}$-$40^{6/7}$), late term ($41^{0/7}$-$41^{6/7}$) and post term (≥$42^{0/7}$) delivery. Hospitalizations of children up to the age of 18 years involving cardiovascular morbidity were evaluated, including structural valvular disease, hypertension, arrhythmias, rheumatic fever, ischemic heart disease, pulmonary heart disease, perimyoendocarditis, congestive heart failure, and others. Kaplan-Meier survival curves were used to compare cumulative hospitalization incidence between groups. A multivariable Weibull parametric model was used to control for confounders.

Results During the study period, 223 242 term singleton deliveries met the inclusion criteria. Of them, 24% (n = 53 501) occurred at early term. Hospitalizations involving cardiovascular morbidity were significantly more common in children delivered at early term (0.7%) as compared with those born at full (0.6%), late (0.6%), or post term (0.5%; $P = .01$). The survival curve demonstrated a significantly higher cumulative incidence of cardiovascular-related hospitalizations in the early term group (log-rank $P < .001$). In the Weibull model, early term delivery was found to be an independent risk factor for cardiovascular-related hospitalization as compared with full term delivery (adjusted HR, 1.16; 95% CI, 1.01-1.32; $P = .02$).

Conclusion Early term delivery is independently associated with pediatric cardiovascular morbidity of the offspring as compared with offspring born at full term. *(J Pediatr 2018;194:81-6).*

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Once considered a homogenous period for delivery with similar expected newborn outcomes, term delivery (defined as delivery between 37 and 42 completed weeks of gestation) is now being closely investigated for different short- and long-term outcomes among offspring according to its subcategories.

In 2005, the designation of "late preterm" infants for those born between 34 and 37 weeks of gestation instead of what was once referred to as "near term" emphasized that these infants may still experience morbidity and mortality traditionally related to prematurity. Later (in 2013), following the recommendations of the "Defining Term Pregnancy workgroup,"[1] the American College of Obstetrics and Gynecology published a new definition of term pregnancy subdividing it to 4 distinct periods: early (between $37^{0/7}$ and $38^{6/7}$ weeks), full (between $39^{0/7}$ and $40^{6/7}$ weeks), late (between $41^{0/7}$ and $41^{6/7}$ weeks), and post (≥$42^{0/7}$ weeks) term.[2] This change in definition was also made based on the realization that fetal maturation continues within term gestation and that early term infants might still be exposed to complications experienced at late preterm deliveries. Recent studies provide increasing evidence that perinatal outcomes of infants delivered at term differ within this 5-week period. The frequency of immediate neonatal adverse outcomes (mainly mortality and respiratory morbidity) seems to be U-shaped, with a nadir around 39-41 weeks of gestation (full term),[3,4] and higher rates observed at early term.

Studies on the long-term outcomes of early term born children previously focused either on respiratory morbidity (including abnormal lung functions,[5] asthma[6] and obstructive sleep apnea[7]) or on neurocognitive development, showing more attention deficit hyperactivity disorder in early term born children[8] and lower school performance and academic achievements.[9,10] The cardiovascular morbidity of early term born infants was not investigated previously. We sought to evaluate whether birth during this early period of term gestation impacts negatively on offspring, similar to the reported respiratory impact, and independent of other pregnancy characteristics, such as birthweight and placental disorders.

ICD-9	*International Classification of Disease, 9th edition*
LMP	Last menstrual period
SUMC	Soroka University Medical Center

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Material and Methods

In this population-based retrospective cohort study, we included all singleton pregnancies of women who delivered at term between 1991 and 2014. The study was conducted at the Soroka University Medical Center (SUMC), the sole tertiary medical center in the Negev (southern Israel) and the largest birth center in the country. Thus, the study is based on nonselective population data.

The institutional review board approved the study that has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments (Helsinki Declaration 1975, revision 2013).

The primary exposure was early term delivery ($37^{0/7}$-$38^{6/7}$ weeks of gestation) as defined by American College of Obstetrics and Gynecology.[2] Gestational age was based on the best obstetrical estimate determined by providers and used for clinical decision making. The standard criteria used involved consideration of the clinical history and earliest ultrasound finding. If the last menstrual period (LMP) was certain and consistent with the ultrasound, dating was based on LMP. If the ultrasound examination was not consistent with the LMP, or the LMP was unknown, ultrasound data were used for determination of gestational age. We excluded multiple pregnancies, preterm deliveries (occurring before 37 completed weeks of gestation) or pregnancies with missing gestational age, perinatal mortality cases (intrauterine fetal death, intrapartum death, and postpartum death), and fetuses with congenital malformations.

A comparison was performed between children born at early term to those born later: at full term, late term, and post-term gestations. Outcomes assessed included adverse perinatal outcome (Apgar score and low birth weight) as well as hospitalizations of the offspring up to the age of 18 years owing to cardiovascular morbidity. A subanalysis using dummy variables was performed to compare full-term offspring with other gestational age study groups. We used the Cox regression model to account for duration of follow-up.

The cardiovascular morbidity diagnoses used were predefined by a set of *International Classification of Disease, 9th edition* (ICD-9) codes detailed in **Table I** (available at www.jpeds.com). Subcategories of cardiovascular morbidity included structural–valvular, hypertension, arrhythmia, rheumatic fever, ischemic heart disease, pulmonary heart disease, perimyoendocarditis, congestive heart failure, heart disease unspecified, and other. The group "other" is a group of diagnoses detailed in the supplement (**Table I**) that constitutes of the list of diagnoses not specified elsewhere in any of the other subgroups, mostly heart murmurs.

Follow-up was terminated if any of the following occurred: first hospitalization for any of the cardiovascular morbidities, hospitalization resulting in death unrelated to cardiovascular morbidity, or when the child reached 18 years of age.

Data were collected from 2 databases that were cross-linked and merged: the computerized hospitalization database of SUMC, and the computerized perinatal database of the obstetrics and gynecology department. The database of SUMC includes demographic information and ICD-9 codes for all medical diagnoses made during hospitalizations in any of the SUMC departments, including the pediatric division. The perinatal database consists of information recorded immediately after delivery by an obstetrician. Experienced medical secretaries routinely review the information before entering it into the database to ensure its maximal completeness and accuracy. Coding is performed after assessing medical prenatal care records as well as routine hospital documents.

Statistical Analyses

Statistical analysis was performed using the SPSS package 23rd edition (IBM/SPSS, Chicago, Illinois) as well as the STATA software 12th edition (StataCorp LLC, College Station, Texas). Categorical data are shown in counts and rates and the differences were assessed by χ^2 for general associations. An ANOVA test was used for comparison of continuous variables with normal distribution. Kaplan–Meier survival curves were used to compare cumulative hospitalization incidences over time among the 4 study groups. Only the first admission with any cardiac-related condition for a given individual was included in the survival analysis. The differences between the 4 curves (according to the different gestational ages) were assessed using the log-rank test.

A multivariable Weibull parametric survival analysis was performed to adjust for duration of follow-up. In this analysis, mothers in the cohort were entered as clusters and the dependence among the siblings was accounted for. The model was constructed to establish an independent association between gestational age at birth and future cumulative cardiovascular hospitalization incidence among the offspring while adjusting for confounding and clinically significant variables, including maternal age, birthweight, maternal hypertensive disorders of pregnancy (chronic hypertension, gestational hypertension, or preeclampsia with or without severe features), maternal diabetes (pregestational and gestational), induction of labor, and mode of delivery. The variables used in the Weibull model were coded as follows: maternal age and birthweight are continuous, and hypertensive disorders, diabetes, induction of labor, and mode of delivery (vaginal or cesarean) are dichotomous. Deliveries occurring at full term (ie, $39^{0/7}$-$40^{6/7}$ weeks) were considered as the reference values. All analyses were 2-sided; $P < .05$ was considered significant.

Results

During the study period, 223 242 deliveries meeting the inclusion criteria occurred at SUMC, of which 53 501 (24%) were early term, 122 602 at full term (54.9%), 37 919 late term (17%), and 9220 at post term (4.1%) gestation. **Table II** summarizes maternal characteristics and immediate perinatal outcomes for the different gestational age groups. Mothers in the early term group were more likely to be diagnosed with hypertensive disorders of pregnancy (chronic hypertension, gestational hypertension, or preeclampsia with or without severe features)

Table II. Maternal characteristics and perinatal outcomes

Maternal Characteristics	Early Term (n = 53 501)	Full Term (n = 122 602)	Late Term (n = 37 919)	Post Term (n = 9220)	*P* value*
Maternal age (years)	28.6 ± 5.9	28.0 ± 5.7	27.9 ± 5.6	28.1 ± 5.7	<.001
Birthweight (g)	3052 ± 450	3292 ± 417	3431 ± 411	3488 ± 430	<.001
Diabetes mellitus† (%)	8.0	4.5	2.3	2.2	<.001
Hypertensive disorders of pregnancy‡ (%)	7.2	4.0	2.9	2.9	<.001
Induction of labor (%)	24.4	24.7	34.0	38.3	<.001
Cesarean delivery (%)	21.8	9.2	9.6	12.6	<.001
Apgar score <7 at 1 minute (%)	3.2	2.6	3.4	5.0	<.001
Apgar score <7 at 5 minutes (%)	0.3	0.2	0.3	0.4	<.001
Low birth weight (<2500 gr) (%)	8.6	2.0	0.9	0.8	<.001

*Calculated for all using the χ^2 test for trends.
†Including pregestational and gestational diabetes.
‡Including chronic hypertension, gestational hypertension, and preeclampsia with or without severe features.

Table III. Long-term cardiovascular morbidities

Cardiovascular morbidities	Early Term (n = 53 501)	Full Term (n = 122 602)	Late Term (n = 37 919)	Post Term (n = 9220)	*P* value*
Structural–valvular	8 (0.01)	29 (0.02)	7 (0.01)	2 (0.02)	.68
Hypertension	37 (0.06)	62 (0.05)	30 (0.07)	7 (0.07)	.16
Arrhythmia†	127 (0.23)	231 (0.18)	78 (0.20)	14 (0.15)	.13
Rheumatic fever	5 (<0.01)	16 (0.01)	9 (0.02)	0 (0)	.17
Ischemic heart disease	2 (<0.01)	1 (<0.01)	1 (<0.01)	1 (0.01)	.19
Pulmonary heart disease	8 (0.01)	12 (<0.01)	3 (<0.01)	1 (0.01)	.73
Perimyoendocarditis‡	26 (0.04)	49 (0.03)	5 (0.01)	3 (0.03)	.04
Congestive heart failure	5 (<0.01)	4 (<0.01)	2 (<0.01)	0 (0)	.35
Heart disease unspecified	4 (<0.01)	4 (<0.01)	4 (0.01)	1 (0.01)	.32
Other§	188 (0.35)	320 (0.26)	103 (0.27)	20 (0.21)	.006
Total hospitalization¶	385 (0.71)	689 (0.56)	224 (0.59)	48 (0.52)	.001

Values are n (%).
*Calculated for all study groups using the χ^2 test for trends.
†*P* value < .05 when early term was compared with full term (HR, 1.35; 95% CI, 1.08-1.67).
‡*P* value < .05 when late term was compared with full tern (HR, 0.30; 95% CI, 0.12-0.76).
§*P* value < .05 when early term was compared with full term (HR, 1.39; 95% CI, 1.16-1.66).
¶*P* value < .05 when early term was compared with full term (HR, 1.34; 95% CI, 1.19-1.52).

and diabetes (pregestational or gestational). Induction of labor rates were comparable between the early term and full-term groups, but significantly more common in the late and post term groups. Cesarean delivery rates were significantly higher in the early term group, as were low Apgar score rates (at 1 and 5 minutes) compared with the full-term group. The mean birth weight was lower at early term compared with later gestational ages.

The long-term cardiovascular hospitalization rates of the offspring are presented in **Table III**. There was a clear trend toward higher specific morbidity rates in the early term group and the overall cardiovascular hospitalization rate up to the age of 18 was significantly higher in the early term delivery group as compared with the full-term group. A subanalysis using dummy variables was performed to compare full-term offspring with the remaining study groups. We used the Cox regression model to account for duration of follow-up and found that arrhythmias (although not significantly different between all groups) are also significantly more prevalent in early term compared with full-term (HR, 1.35; 95% CI, 1.08-1.67) cohorts, as are other diagnoses (HR, 1.39; 95% CI, 1.16-1.66). In contrast, we found that perimyocarditis was not different between the early term and full-term groups, and that being born at late term had a protective effect compared with full term (HR, 0.30; 95% CI, 0.12-0.76). A χ^2 test for trends confirmed a linear-by-linear association with a "dose-dependent" effect; as gestational age within term advanced, the risk for future cardiovascular-related hospitalizations decreased.

In the Kaplan–Meier survival curve (**Figure**), children born at early term had a significantly higher cumulative incidence of hospitalizations owing to cardiovascular morbidity, as compared with children born at full, late, or post term ($P < .001$).

Table IV presents the multivariable Weibull parametric survival analysis for the association between long-term risk for

Table IV. Multivariable Weibull parametric survival analysis

	HR	95% CI	*P* value
Early term	1.16	1.01-1.32	.028
Full term	1.0 (Reference)	-	-
Late term	1.09	0.94-1.27	.25
Post term	1.07	0.79-1.44	.65

Controlled for maternal age, birthweight, diabetes mellitus (including pregestational and gestational), hypertensive disorders (including pregestational and gestational diabetes, and preeclampsia with or without severe features), induction of labor, and cesarean delivery.

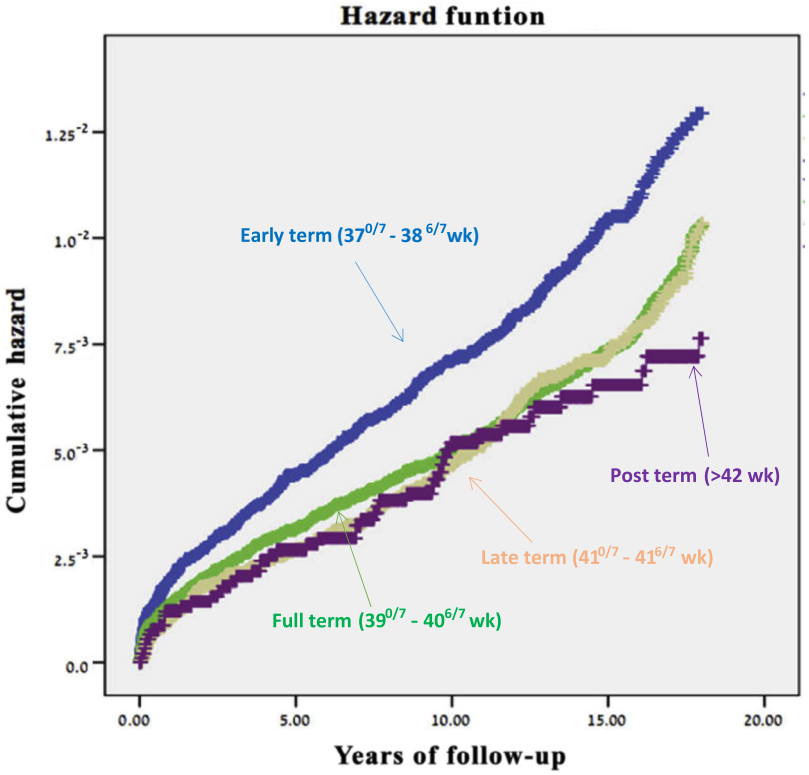

Figure. Kaplan–Meier survival curve. Cumulative incidence of cardiovascular hospitalizations in children up to 18 years of age according to gestational age at birth. Total cardiovascular hospitalizations (log-rank $P < .001$).

cardiovascular-related hospitalizations in children (up to 18 years of age) and gestational age at term birth. The model was adjusted for maternal age, birthweight, hypertensive disorders of pregnancy, maternal diabetes, mode of delivery, and induction of labor. Compared with full-term delivery, early term delivery exhibited a significant and independent association with the long-term risk for cardiovascular-related hospitalization of the offspring with an adjusted HR of 1.16 (95% CI, 1.01-1.32; $P = .028$).

Discussion

The immediate and long-term consequences of early term deliveries are now starting to surface in the scientific obstetrical and pediatric literature, as more and more studies suggest an increased risk for neonatal mortality and long-term morbidity. Respiratory, neurologic, and developmental morbidities were all suggested to be more prevalent in this group of children born at early term when compared with full-term born children. Our study now adds to the existing literature by suggesting an increased risk for pediatric cardiovascular morbidity in this possibly vulnerable subgroup of children, which is likely to affect adult life as well.

It has been shown that early term delivery is associated independently with increased perinatal mortality,[11,12] as well as increased mortality during infancy, early childhood, and young adulthood.[13] In the latter study, Crump et al found early term delivery to be associated with a higher risk for all-cause mortality and, when examined according to cause, a possible increased risk for cardiovascular mortality in those 18-36 years of age was suggested for individuals born at early term.[13] Although not without limitations, this finding highlights the important role of cardiovascular disorders later in life among offspring born at early term.

Our study found that children born at early term had a significantly higher risk to be hospitalized owing to a cardiovascular-related diagnoses compared with children born at full term. This pattern resembles that in other childhood morbidities related to early term delivery, mainly respiratory and neurocognitive issues. Our group previously investigated the negative impact of early term delivery on the long-term respiratory health of the offspring with a wide variety of respiratory morbidities found to be more common in this group of offspring.[6,7] In addition, clues of long-term abnormal development of early term infants were demonstrated in a meta-analysis,[14] with poorer outcomes in school performance and other important neurologic determinants.

The origins of the increased morbidities for term born offspring are still under investigation. Possible explanations may relate to fetal programming, an emerging concept linking environmental conditions during embryonic and fetal development with the risk of disease later in life. From a cardiovascular point of view, the "fetal origins of adult disease hypothesis"

originally described by Barker et al identified the relationship between impaired in utero growth and an increased risk for later adult cardiovascular disease and death.[15] Barker et al postulated that a process of "fetal programing" to adapt to in utero conditions increases the risk for higher blood pressure and cardiovascular disease after birth. Since then, the correlation between intrauterine growth restriction and future cardiovascular disease was repeatedly established by multiple epidemiologic and prospective studies.[16-19]

The Barker hypothesis may help in shedding some light on our findings. Importantly, infants born at early term in our cohort were, as expected, more likely to have lower birthweights. Low birthweight, in return, is linked with future cardiovascular health of the offspring, as discussed. Nevertheless, the Weibull model designated to control for birthweight demonstrated early term delivery to be independently associated with future cardiovascular morbidity, as compared with full-term delivery. Thus, birthweight does not seem to provide the entire explanation. Other obstetric risk factors for future cardiovascular disease of the offspring are maternal hypertensive disease[20] and maternal diabetes.[21] In their 2014 review, Herrera-Garcia and Contag focused on hypertensive disease of pregnancy and confirmed maternal hypertensive disease to be associated with an increased lifetime cardiovascular risk in the offspring, including stroke, myocardial disease, coronary artery disease, and peripheral arterial disease.[22] Maternal diabetes is another risk factor for future metabolic complications in the offspring, such as obesity and diabetes.[23-26] Again, these conditions may impact, in return, cardiovascular function in the child. In our cohort, both of these morbidities were more common in the early term group than in later gestational age groups. This finding is expected, because both conditions often lead to medically indicated deliveries at early term. However, we were careful in controlling for these factors in our Weibull model; even so, the link between early term delivery and long-term cardiovascular morbidity remained significant.

One must consider the indication for early term induction of labor (hypertensive disease or maternal diabetes) as a possible cause for the findings. In our cohort, labor induction rates were almost identical in the early term and full-term groups, but the long-term outcomes differed significantly. Moreover, the Weibull model found gestational age at delivery (early term) to be independently associated with an increased risk for cardiovascular hospitalizations after controlling not only for maternal hypertensive disorders and diabetes mellitus, but also for labor induction itself. Maternal age (also considered as a potential confounder) was statistically different between gestational age groups, but this seems to have minimal clinical implications, because mean age was roughly 28 years for all groups. Apgar scores were statistically different between groups but, again, their impact on long-term cardiac health of the offspring is less clear.

Prematurity (delivery before 37 weeks of gestation) is a known risk factor for future cardiovascular morbidity of the preterm infant, and specifically hypertension disorders later in life, with several prospective studies and meta-analyses[27-30] suggesting this link. Bayman et al found evidence of vascular endothelial changes in preterm offspring (such as increased intima media thickness as an early sign of atheroma formation[28]) that are associated with hypertension, dyslipidemia, and increased body mass index.[31] Prematurity has also been linked to insulin resistance and future development of type 2 diabetes,[32] suggesting that insulin resistance may be present from early life.[33] Finally, research on the preterm heart reveals that individuals born preterm have increased left ventricular mass and smaller right ventricular size in adult life. Furthermore, they exhibit a unique 3-dimensional left ventricular geometry and significant reductions in systolic and diastolic functional parameters.[34,35] Although the pathophysiology underlying increased rates of morbidities in early term deliveries is not fully elucidated, it is suggested that early term is part of a "continuum of prematurity." It is reasonable to assume that the maturation of the cardiovascular system follows the same logic.

This study evaluated cardiovascular health in early term born children; the main strength lies in its nonselective, population-based large cohort and having been able to combine databases from the obstetrical department and the entire hospitals records. We were able to prospectively analyze the data to reveal the long-term risk, and establish a "dose-dependent" effect showing that, as gestational age increases, even within term, the risk for future hospitalization gradually decreases. The main limitation of our study lies within its retrospective design. As a population-level analysis, our study can provide evidence only of association and not of causation. Nevertheless, there seems to be a biological plausibility and we believe that early term born infants are not fully mature and that their cardiovascular function exhibits characteristics of prematurity. Our study reinforces current recommendations to avoid, when possible, elective early term deliveries because gestational age seems to account for part of the long-term morbidities seen in this group of offspring. ■

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Table I. ICD-9 codes used

Groups	Diagnostic Code	Diagnosis Description
Structural valvular disease	3940	Mitral stenosis
	3949	Other and unspecified mitral valve diseases
	3961	Mitral valve stenosis and aortic valve insufficiency
	3963	Mitral valve insufficiency and aortic valve insufficiency
	3968	Multiple involvement of mitral and aortic valves
	3970	Diseases of tricuspid valve
	4240	Mitral valve disorders
	4241	Aortic valve disorders
	4242	Tricuspid valve disorders, specified as nonrheumatic
	4243	Pulmonary valve disorders
Hypertension	4019	Unspecified essential hypertension
	4372	Hypertensive encephalopathy
	40390	Unspecified hypertensive kidney disease with chronic kidney disease stage I through stage IV, or unspecified
	40391	Unspecified hypertensive kidney disease with chronic kidney disease
	40391	Unspecified hypertensive kidney dis. with chronic kidney disease stage V or end-stage renal disease
	40391	Unspecified hypertensive renal dis. + renal failure
	40591	Unspecified renovascular hypertension
Arrhythmia	4260	Atrioventricular block, COMPLETE
	4263	Other left bundle branch block
	4264	Right bundle branch block
	4267	Anomalous atrioventricular excitation
	4270	Paroxysmal supraventricular tachycardia
	4271	Paroxysmal ventricular tachycardia
	4272	Paroxysmal tachycardia, unspecified
	4273	Atrial fibrillation and flutter
	4275	Cardiac arrest
	4279	Cardiac dysrhythmia, unspecified
	7850	Tachycardia, unspecified
	7851	Palpitations
	42611	First-degree atrioventricular block
	42612	Mobitz (type) II atrioventricular block
	42613	Other second-degree atrioventricular block
	42682	Long QT syndrome
	42689	Other specified conduction disorders
	42731	Atrial fibrillation
	42732	Atrial flutter
	42741	Ventricular fibrillation
	42760	Premature beats, unspecified
	42761	Supraventricular premature beats
	42769	Other premature beats
	42789	Other specified cardiac dysrhythmias
	427811	Sinus bradycardia
	42671	Wolff-Parkinson-White syndrome
Rheumatic fever	390	Rheumatic fever without mention of heart involvement
	3911	Acute rheumatic endocarditis
	3918	Other acute rheumatic heart disease
	3919	Acute rheumatic heart disease, unspecified
	3920	Rheumatic chorea with heart involvement
	3929	Rheumatic chorea without mention of heart involvement
	3941	Rheumatic mitral insufficiency
	3951	Rheumatic aortic insufficiency
	39890	Rheumatic heart disease, unspecified
Ischemic heart disease	414	Other forms of chronic ischemic heart disease
	4100	Acute myocardial infarction of anterolateral wall
	4109	Acute myocardial infarction of unspecified site
	4111	Intermediate coronary syndrome
	4149	Chronic ischemic heart disease, unspecified
	4292	Cardiovascular disease, unspecified
	4295	Rupture of chordae tendineae
	41000	Acute myocardial infarction anterolateral, episode of care unspecified
	41011	Acute myocardial infarction other anterior, initial episode of care
	41071	Acute myocardial infarction subendocardial, initial episode of care
	41091	Acute myocardial infarction unspecified site, initial episode of care
	41410	Aneurysm of heart (wall)
	42979	other, mural thrombus (atrial) (ventricular) acquired, following myocardial infarction

(*continued*)

Table I. Continued

Groups	Diagnostic Code	Diagnosis Description
Pulmonary heart disease	4160	Primary pulmonary hypertension
	4168	Other chronic pulmonary heart diseases
	4169	Chronic pulmonary heart disease, unspecified
	4171	Aneurysm of pulmonary artery
	41512	Septic pulmonary embolism
	41519	Other pulmonary embolism and infarction
Perimyoendocarditis	4210	Acute and subacute bacterial endocarditis
	4211	Acute and subacute infectious endocarditis in disease classified elsewhere
	4230	Hemopericardium
	4232	Constrictive pericarditis
	4233	Cardiac tamponade
	4238	Other specified diseases of pericardium
	4239	Unspecified disease of pericardium
	4251	Hypertrophic obstructive cardiomyopathy
	4252	Obscure cardiomyopathy of Africa
	4253	Endocardial fibroelastosis
	4254	Other primary cardiomyopathies
	4257	Nutritional and metabolic cardiomyopathy
	4259	Secondary cardiomyopathy, unspecified
	4289	Heart failure, unspecified
	4290	Myocarditis, unspecified
	42090	Acute pericarditis, unspecified
	42099	Other acute pericarditis
	42290	Acute myocarditis, unspecified
	42291	Idiopathic myocarditis
	42292	Septic myocarditis
	42490	Endocarditis, valve unspecified, unspecified cause
Heart failure	4280	Congestive heart failure
	4280	Congestive heart failure, unspecified
	4281	Left heart failure
	42841	Acute combined systolic and diastolic heart failure
Heart disease not otherwise specified	4299	Heart disease, unspecified
	9971	Cardiac complications, not elsewhere classified
	42989	Other ill-defined heart diseases
Other	7852	Functional and undiagnosed cardiac murmurs
	7852	Undiagnosed cardiac murmurs (heart murmur not otherwise specified)
	7859	Other symptoms involving cardiovascular system
	78521	Systolic murmur