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Nationwide study of TPE vs IVIG in Guillain-Barré Syndrome

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Abstract

Introduction: We compared outcomes of therapeutic plasma exchange (TPE) versus intravenous immunoglobulin (IVIG) among hospitalized patients diagnosed with Guillain-Barré Syndrome (GBS)

Methods: In a retrospective cohort study of 6,642 records (2,637 TPE and 4,005 IVIG) from the 2002-2014 Nationwide Inpatient Sample, treatment type was examined as predictor of length of stay, total charges and in-hospital death with regression modeling using risk adjustment and propensity scoring to control for confounders.

Results: Compared to those receiving IVIG, patients who underwent TPE experienced prolonged hospitalization by about 7.5 days, greater hospitalization costs by approximately $46,000, and increased in-hospital death with an odds ratio of 2.78. Results did not change after controlling for confounders through risk adjustment, propensity score adjustment or matching.

Discussion: TPE may be associated with poorer healthcare utilization outcomes versus IVIG, although confounding by indication could not be ascertained.

Keywords

Autoimmunity; Guillain-Barré Syndrome; Healthcare utilization; Immunotherapy; Intravenous immunoglobulin; Therapeutic plasma exchange

INTRODUCTION:

According to evidence-based guidelines by the American Academy of Neurology, the two recommended treatment options for severely-affected Guillain-Barré Syndrome (GBS)

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patients are therapeutic plasma exchange (TPE) and intravenous immunoglobulin (IVIG).[1,2] Both treatments were shown to be effective and superior to conservative treatment for disability recovery.[2] Although TPE was shown to be safe and less expensive when administered by experienced physicians, IVIG is preferred by most physicians because of its ease of administration and lower likelihood of complications.[2,3] Nevertheless, it is estimated that approximately 20% of patients with GBS may have severe disability, and 4-15% may die despite close monitoring and administration of immunotherapeutic treatments, including TPE or IVIG.[2,4]

Recently published comparative and non-comparative studies of GBS outcomes after treatment with TPE and/or IVIG have consisted primarily of case reports or case series from single institutions in developing countries, at which the choice between TPE and IVIG is largely dependent on economic considerations.[1-23] Given the established equivalence between TPE and IVIG as effective treatments for GBS, it is important to evaluate patient- and hospital-level characteristics that may affect treatment selection. Also, given the acute nature of GBS and the increased morbidity and mortality risks among GBS-diagnosed patients, it is imperative to examine healthcare utilization outcome differences between TPE and IVIG treatments. The purpose of this study is to compare healthcare utilization outcomes of TPE versus IVIG among hospitalized patients diagnosed with GBS. We hypothesized that TPE and IVIG had similar profiles in terms of healthcare utilization outcomes in the context of GBS.

METHODS:

Data source:

The Agency for Healthcare Research and Quality (AHRQ) Healthcare Cost and Utilization Project (HCUP) consists of publicly available databases and software tools in the United States. It comprises all-payer, encounter-level information that can be used to support decision-making and enable research at national, state, and local levels. Initiated in 1988, the HCUP Nationwide Inpatient Sample (NIS) was designed to yield national estimates focused on hospital inpatient stays, including health care utilization, access, charges, quality and outcomes. A 20% stratified random sample is selected on an annual basis from the HCUP State Inpatient Databases which include the universe of inpatient discharge abstracts from participating states. Before 2012, the sampling frame for HCUP-participating hospitals was divided into multiple strata according to hospital characteristics (ownership/control (government, nonfederal; private, non-profit; private, investor-own), bed size (small; medium; large), teaching status (non-teaching, teaching), location (urban; rural), Census regions (4 before 2012: Northeast; Midwest; South; West; 9 in 2012 or later: New England; Middle Atlantic; East North Central; West North Central; South Atlantic; East South Central; West South Central; Mountain; Pacific), and samples of hospital discharge records were selected with probabilities proportionate to the number of hospitals within each of the five stratifying variables. Since 2012, the 20% NIS sampling strategy has shifted from the selection of hospitals from which all hospital discharge records were kept to the selection of hospital discharge records, with probabilities of selection proportionate to the number of hospital discharge records per stratum. All statistical analyses were performed taking the

NIS sampling strategies into consideration, including the use of discharge weight (DISCWT) to project discharges in the NIS data files to discharges from all U.S. community hospitals, excluding rehabilitation and long-term acute care hospitals. The NIS databases contain data elements typical of a discharge abstract, including patient- and hospital-level characteristics.

Study population and sample:

Secondary analyses were performed using the 2002-2014 NIS data, with specific eligibility criteria applied to define the study population on the basis of the International Classification of Diseases 9th Revision, Clinical Modification (ICD-9-CM) diagnostic and procedure codes. The unselected sample consisted of 101,231,036 hospital discharges for the 12-year time period, representing 482,872,274 hospital discharges at the national level. Of those, 39,452 corresponded to patients having a GBS diagnosis on the basis of having a primary or a secondary ICD-9-CM code of 357.0. Among these records, 32,490 were excluded because IVIG (99.14) or TPE (99.71) were not performed and 320 were excluded because they corresponded to patients who were simultaneously treated with IVIG and TPE, after reviewing up to 15 ICD-9-CM procedure codes. The final study sample consisted of 2,637 records for patients treated with TPE alone and 4,005 records for patients treated with IVIG alone (Supplemental Figure 1). Of those, 6,586 (2,617 TPE and 3,969 IVIG) had no missing data on key variables of interest, including patient and hospital characteristics as well as healthcare utilization outcomes, and were used in subsequent analyses.

Patient and hospital characteristics:

Comparisons between TPE and IVIG treatment groups on several patient- and hospital-level characteristics were performed. These same variables were examined as potential confounders for the exposure-outcome relationships of interest. Patient-level characteristics were defined as age, race/ethnicity, Charlson comorbidity index (CCI), year of admission, admission quarter, weekend admission status and primary payer. Hospital-level characteristics were defined as hospital region, location and teaching status as well as bed size.

Healthcare utilization outcomes:

Treatment type (TPE vs. IVIG) was examined in relation to several healthcare utilization outcomes, defined using existing data elements from the NIS database, including in-hospital death status (“yes” or “no” (referent)), length of hospital stay (in days) and hospital charges (in U.S. dollars, adjusted for 2002-2014 inflation rates).[24] The two continuous outcomes (length of hospital stay and hospital charges) were $\log_e$-transformed in the context of regression analysis because of their skewed distributions. We also described and compared discharge destination among recipients of TPE and IVIG.

Statistical analysis:

All statistical analyses were conducted using STATA version 15 (StataCorp, College Station, TX), taking complex survey design into consideration, including the use of DISCWT. Descriptive statistics included mean (± standard error) for continuous variables and frequencies with percentages for categorical variables. Bivariate associations were examined

using uncorrected Chi-square and design-based F-tests. Linear and binary logistic regression models were constructed to estimate crude and adjusted beta coefficients as well as odds ratios (cOR and aOR) with their 95% confidence intervals (CI) for exposure variables as predictors of the selected health outcomes. First, we compared TPE and IVIG groups on patient- and hospital-level characteristics. Second, we examined the relationship between treatment type and healthcare utilization outcomes, namely, in-hospital death status, $\log_e$-transformed length of stay and $\log_e$-transformed hospital charges (adjusted for inflation using the Consumer Price Index), before and after controlling for confounders using risk-adjustment as well as propensity scoring. We also examined effect modification of exposure-outcome relationships by sex and time period (2002-2007, 2008-2014) within regression models. Complete subject analyses were performed based on available sub-samples for variables under evaluation. Two-sided statistical tests were conducted and after Bonferroni correction for 50 hypothesis tests, α=0.001 was considered statistically significant.

Propensity score methodology:

Propensity scoring is an alternative method to multivariable regression modeling and a powerful tool for making causal inferences drawn from observational studies. Furthermore, propensity scoring can ensure that treatment groups have equal distribution on patient characteristics affecting outcome (e.g. age, gender, comorbidities, etc.) and that differences in outcomes between various treatments can be attributed to treatment.[25,26] In this study, we calculated propensity scores or predicted probabilities of treatment type for each hospitalization based on a set of relevant characteristics using a two-step procedure: (1) treatment type was modeled as the outcome variable in a multiple logistic regression model including as predictor variables a selected group of patient- and hospital-level covariates that were identified as key confounders of the exposure-outcome association; (2) predicted probabilities of treatment type (“propensity scores”) were used as a covariate in regression models that examined the relationship between treatment type and healthcare utilization outcomes (propensity score adjustment) or were used for the creation of a matched sample (propensity score matching).

A patient- or hospital-level characteristic was identified as a key confounder if the following criteria were met: (1) Relationship between covariate and treatment type is statistically significant; (2) Relationship between covariate and healthcare utilization outcome is statistically significant; (3) A ±5% change in effect estimate (exposure-outcome relationship) was observed between a regression model that includes treatment type as a predictor of healthcare utilization outcome and a regression model that includes treatment type and the covariate as predictors of healthcare utilization outcome (Supplemental Table 1). Accordingly, a total of 7 covariates (age; race; CCI; admission status; year of admission; primary payer; hospital region) were initially included in the propensity score model. Of those, 3 variables (age; CCI; admission status) remained in this model in order to ensure that propensity scores were balanced across treatment and comparison groups and that covariates were balanced between treatment and comparison groups within blocks of the propensity score, before and after creation of a matched sample.

RESULTS:

Approximately 56% of hospital discharges corresponded to male patients, 59% to those between 30 and 79 years of age and 47% to those of White race. Furthermore, 62% had a CCI score of zero and 89% had a non-elective hospitalization. Patients older than 10 years of age were increasingly more likely to receive TPE (versus IVIG). Moreover, recipients of TPE were more likely to have a CCI score that was greater than zero and to receive non-elective treatment than IVIG recipients. By contrast, utilization of TPE appeared to decrease over the years, and was less frequently utilized in the Northeast and in rural areas. Of 6,586 patients from the study sample, 5,166 had known discharge destination, including vital status and location (Tables 1-2 and Supplemental Table 2).

Two multiple logistic regression models (Model I and Model II) were evaluated for the generation of propensity scores. Model I includes covariates that were individually found to be key confounders for at least one of the three exposure-outcome relationships. This model which included age group, race/ethnicity, CCI, admission status, year of admission, primary payer and hospital region was unbalanced. Model II was generated from Model I after serial exclusion of covariates according to their potential of confounding bias by examination of percentage change in the effect estimate of the exposure-outcome relationship. This model which included age group, CCI and admission status as covariates resulted in balancing of propensity scores between the treatment groups (TPE vs. IVIG) as well as balancing of covariates between treatment groups within propensity score blocks, either before or after propensity score matching. Thus, covariates kept in Model II were used for risk-adjustment, propensity score adjustment and propensity score matching (Supplemental Table 3).

The average length of hospital stay for patients undergoing any of the two immunotherapies was 13.22 (95% CI: 12.86, 13.59) days, with significant differences between TPE (17.78 (95% CI: 17.07, 18.49) days) and IVIG (10.24 (95% CI: 9.87, 10.61) days) recipients. Similarly, total hospital charges were estimated at $122,924 (95% CI: $119,067, $126,782) per hospital discharge, with significantly greater charges among TPE ($149,143 ($142,615, $155,669)) than IVIG ($103,223 ($98,753, $107,693)) recipients. Finally, a total of 154 in-hospital deaths were reported, with an estimated death rate of 2.4% (95% CI: 2.0%, 2.8%) and a significantly higher death rate among recipients of TPE (3.8%, 95%CI: 3.2%, 4.7%) than IVIG (1.4%, 95% CI: 1.0%, 1.8%).

Tables 3-5 present linear and logistic regression models for treatment type as a predictor of $\log_e$-transformed length of stay, $\log_e$-transformed total hospitalization charges and in-hospital death, before and after controlling for confounders, and stratifying by sex. For propensity score matching, the matched sample consisted of 6,578 for length of hospital stay, 6,414 for total hospital charges and 6,570 for in-hospital death. Furthermore, TPE was associated with prolonged hospital stay, greater hospitalization charges and poorer outcome in terms of in-hospital death as compared to IVIG, in the unadjusted and adjusted models. Results from risk-adjusted, propensity score adjusted and propensity score matched models were also consistent among each other. For hospitalization charges and in-hospital death, but not for length of hospital stay, propensity-score adjusted models yielded more conservative estimates as compared to risk-adjusted models. There were no statistically

significant interaction effects between treatment and sex or between treatment and time period in relation to the three outcomes of interest.

DISCUSSION:

This study found that patients who underwent TPE (versus IVIG) experienced prolonged hospitalization by an average of about 7.5 days, greater hospitalization costs on an average of approximately $46,000, and worsened outcome in terms of in-hospital death with OR = 2.78 (95% CI: 1.99, 3.88). These results did not change after controlling for key confounders through risk adjustment, propensity score adjustment or propensity score matching. It is worth noting that both TPE and IVIG are frequently administered under specific universal protocols and as such one difference is that TPE administration requires routinely 8-10 days whereas IVIG is commonly administered over 5 days. However, treatment patterns differ between hospitals and often differ from standard published protocols. For instance, it is not uncommon for IVIG to be given as a standard dose (2 gm/kg) divided over 2-3 days rather than 5 days, in order to reduce the consumption of healthcare resources. Accordingly, differences in length of stay and hospitalization costs between these two treatments are expected, whereas differences in survival necessitate in-depth investigation. These results appear to be homogeneous when stratifying by sex and time period. Nevertheless, interpretation of these subgroup analyses should take into account the limitations described by Rothwell et al., especially the extent of pathophysiologic differences between males and females affected by GBS and changes in treatment guidelines and practices over time.[27]

Current evidence in support of using either of these two treatments has been summarized in two systematic reviews and meta-analyses.[28,29] One meta-analysis found no difference between TPE and IVIG in any of the primary or secondary outcomes, including a seven-grade disability scale at 4 weeks of follow-up.[29] Another meta-analysis indicated that patients assigned to IVIG were significantly less likely to discontinue treatment than those assigned to TPE.[28]

Previous studies primarily described outcomes of one of these two treatments using case series of patients diagnosed with GBS and/or similar conditions from a single institution. These studies often originated from developing countries. [1-3,18,22] For instance, a retrospective study involving 230 South Indian TPE-treated patients diagnosed with neurological disorders reported that GBS was a key diagnosis.[2] Their study found no deaths had occurred post-TPE treatment.[2] Nizar *et al.* examined a case series of 192 TPE procedures on 40 patients from a Nephrology Department in South India, of which two-thirds had GBS.[3] Overall, 36 patients showed significant improvement in their condition, 2 did not show any change, 1 worsened and 1 died due to respiratory complications.[3] A case series by Vikrant *et al.* involving 120 TPE sessions performed among 31 GBS patients reported 1 death, for a mortality risk of 3.2%.[3] Saad *et al.* retrospectively evaluated 62 children with GBS from Upper Egypt, comparing treatment outcomes of 32 patients who underwent TPE with those of 30 patients who received IVIG.[18] Unlike our study, theirs suggested no difference in mortality risks between the two treatment modalities, although those who received IVIG had prolonged hospitalization, were less likely to recover and more likely to require mechanical ventilation than those who underwent TPE.[18]

Our study findings should be interpreted with caution and in light of several limitations. First, the NIS is an administrative database of hospital discharge records with limited scope, accuracy and completeness as well as limited information pertaining to reason for hospital admission, laboratory tests and medications. Second, data clustering as a result of patient re-admission to one of the participating hospitals cannot be evaluated in the absence of unique patient identifiers. Third, complete subject analysis was performed with potential for selection bias because of missing exposure, outcome and/or covariate data. Fourth, eligibility criteria and many of the study variables were defined on the basis of ICD-9-CM codes, potentially leading to misclassification bias. Fifth, unmeasured confounders may have led to residual confounding despite efforts at using advanced techniques such as propensity scoring. In particular, disease severity could not be ascertained in the context of this administrative database, although patients who underwent immunotherapeutic treatments were likely experiencing acute symptoms of GBS. Furthermore, the choice between these two treatments often depends on unmeasured variables such as local availability, patient preference, risk factors and contraindications. Whereas two healthcare utilization outcomes (length of stay and charges) are easily explained by differences in the selected GBS therapies, the finding of increased in-hospital mortality among TPE vs. IVIG may be attributed to confounding by indication, and this cannot be determined using the data elements within the NIS database. Sixth, the study design does not allow for the longitudinal examination of outcomes beyond hospitalization or the establishment of a temporal sequence of events, with the exception of discharge-related outcomes, e.g. length of hospital stay, hospital charges and in-hospital death, which are known to have occurred following diagnosis and procedures. It is worth noting that rare outcomes such as specific complications could not be examined in relation to treatment type due to sample size limitations. By contrast, multiple comparisons using a relatively large sample may have yielded statistically though not clinically significant findings. Also, a fixed sample size of > 6,000 hospital discharge records had sufficient power to detect hypothesized differences in healthcare utilization outcomes between TPE and IVIG groups as well as interaction effects by sex and time period with a power of nearly 100%. Finally, the results of this study can only be generalized to hospitalized patients, whose characteristics may differ from those who sought outpatient care.

In conclusion, TPE may be associated with poorer healthcare utilization outcomes compared to IVIG, regardless of the method applied to control for confounders, although confounding by indication could not be ascertained. Comparative safety and effectiveness studies are needed to confirm these preliminary findings, using large prospective cohort designs with the capability to control for additional prognostic factors and a longer-term follow-up period.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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List of Acronyms and Abbreviations:

AHRQ	Agency for Healthcare Research and Quality
CCI	Charlson comorbidity index
CI	Confidence intervals
HCUP	Healthcare Cost and Utilization Project
ICD-9-CM	International Classification of Diseases 9th Revision, Clinical Modification
IVIG	Intravenous immunoglobulin
NIS	Nationwide Inpatient Sample
OR	Odds ratios
TPE	Therapeutic plasma exchange

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Table 1.

Treatment Type by Patient Characteristics – 2002-2014 Nationwide Inpatient Sample (n= 6,586)

	Total (n=6,586)	TPE (n=2,617)		IVIG (n=3,969)		cOR (95% CI)
	N (%)	N	%	N	%	
Sex:						
Male	3,711 (56.3)	1,482	56.7	2,229	56.2	Ref.
Female	2,875 (43.6)	1,135	43.3	1,740	43.8	0.98 (0.88, 1.08)
Age (years):						
< 10	240 (3.6)	15	0.6	225	5.6	Ref.
10-19	346 (5.3)	84	3.2	262	6.6	4.80 (2.69, 8.58)
20-29	420 (6.4)	185	7.1	235	5.9	12.02 (6.87, 21.03)
30-39	598 (9.1)	258	9.9	340	8.5	11.51 (6.64, 19.93)
40-49	799 (12.1)	387	14.7	412	10.4	14.09 (8.19, 24.24)
50-59	942 (14.2)	427	16.3	515	12.9	12.58 (7.33, 21.59)
60-69	916 (13.8)	436	16.6	480	12.0	13.72 (7.99, 23.55)
70-79	649 (9.8)	322	12.2	327	8.2	14.75 (8.54, 25.47)
80+	1,676 (25.7)	503	19.4	1,173	29.8	6.48 (3.79, 11.05)
Race / Ethnicity:						
White	3,117 (47.2)	1,303	49.7	1,814	45.6	Ref.
Black	383 (5.8)	165	6.2	218	5.5	1.04 (0.84, 1.29)
Hispanic	458 (6.9)	189	7.1	270	6.8	0.96 (0.79, 1.17)
Other	315 (4.8)	121	4.6	194	4.9	0.87 (0.68, 1.10)
Unknown	2,312 (35.3)	839	32.4	1,473	37.2	0.79 (0.71, .89)
Charlson Comorbidity Index:						
0	4,081 (62.0)	1,481	56.6	2,600	65.5	Ref.
1	1,299 (19.7)	575	21.9	724	18.2	1.39 (1.22, 1.58)
2+	1,206 (18.3)	561	21.4	645	16.2	1.53 (1.34, 1.74)
Admission status:						
Non-elective	5,850 (88.9)	2,280	87.2	3,570	90.0	Ref.
Elective	735 (11.1)	336	12.8	399	9.9	1.32 (1.13, 1.55)
Primary payer:						
Medicare	1,829 (27.7)	816	31.0	1,013	25.5	Ref.
Medicaid	798 (12.2)	274	10.5	524	13.3	0.65 (0.54, .77)
Private insurance	3,339 (50.8)	1,288	49.4	2,051	51.7	0.79 (0.69, .88)
Self-Pay	365 (5.5)	137	5.3	228	5.7	0.76 (0.59, .95)
No charge	16 (0.2)	***	0.1	12	0.3	0.39 (0.13, 1.25)
Other	239 (3.6)	98	3.8	141	3.5	0.88 (0.67, 1.16)
Discharge destination:						
Routinely discharged	1,909 (36.9)	645	29.0	1,264	42.9	Ref.
Transferred to short-term hospital	221 (4.3)	99	4.5	122	4.3	1.58 (1.19, 2.10)
Transferred to other type of facility	2,446 (47.3)	1,189	53.4	1,257	47.3	1.85 (1.64, 2.09)
Received home healthcare	457 (8.9)	198	8.9	259	8.9	1.49 (1.21, 1.84)

	Total (n=6,586)	TPE (n=2,617)		IVIG (n=3,969)		cOR (95% CI)
	N (%)	N	%	N	%	
Discharged again medical advice	*** (0.2)	***	0.2	***	0.2	1.88 (.46, 7.59)
Died while hospitalized	120 (2.3)	83	3.8	37	2.3	4.52 (3.03, 6.75)
Discharged alive with unknown destination	*** (0.09)	***	0.1	***	0.0	2.64 (.44, 15.93)

Abbreviations: CI=Confidence Interval, cOR=crude odds ratio, IVIG=Intravenous Immunoglobulin. *** Less than 10 hospital discharge records.

Table 2.

Treatment Type by Hospital Characteristics – 2002-2014 Nationwide Inpatient Sample (n= 6,586)

	Total (n=6,586)	TPE (n=2,617)		IVIG (n=3,969)		cOR (95% CI)
	N (%)	N	%	N	%	
Hospital region:						
Northeast	1,440 (22.5)	446	17.7	994	25.7	Ref.
Midwest	1,334 (20.4)	691	26.7	643	16.2	2.39 (2.06, 2.79)
South	2,425 (36.3)	938	35.2	1,487	36.9	1.39 (1.21, 1.59)
West	1,387 (20.9)	542	20.4	845	21.1	1.41 (1.21, 1.64)
Location and teaching status:						
Rural	258 (3.9)	77	2.9	181	4.7	Ref.
Urban – Non-Teaching	1,913 (28.7)	840	31.7	1,073	26.7	1.93 (1.46, 2.53)
Urban – Teaching	4,392 (67.4)	1,694	65.4	2,698	68.6	1.55 (1.19, 2.02)
Hospital bed size:						
Small	495 (7.2)	175	6.3	320	7.7	Ref.
Medium	1,327 (20.3)	514	19.8	813	20.7	1.17 (.95, 1.45)
Large	4,741 (72.5)	1,922	73.9	2,819	72.5	1.27 (1.05, 1.53)

Abbreviations: CI=Confidence Interval, cOR=crude odds ratio, IVIG=Intravenous Immunoglobulin.

Table 3.

Linear regression models for treatment type as a predictor of $\log_e$-transformed length of stay – 2002-2014 Nationwide Inpatient Sample *

TPE vs. IVIG: †	**β**	**95% CI**
OVERALL:		
Model 1 – Unadjusted	0.56	0.52, 0.59
Model 2 – Risk-Adjusted	0.53	0.49, 0.58
Model 3 – Propensity-score adjusted	0.54	0.50, 0.58
Model 4 – Propensity-score matched	0.56	0.52, 0.61
MALE:		
Model 1 – Unadjusted	0.56	0.51, 0.62
Model 2 – Risk-Adjusted	0.53	0.47, 0.59
Model 3 – Propensity-score adjusted	0.54	0.48, 0.59
Model 4 – Propensity-score matched	0.56	0.51, 0.62
FEMALE:		
Model 1 – Unadjusted	0.56	0.50, 0.63
Model 2 – Risk-Adjusted	0.54	0.48, 0.61
Model 3 – Propensity-score adjusted	0.55	0.48, 0.61
Model 4 – Propensity-score matched	0.56	0.49, 0.63
Period 1 (2002-2007):		
Model 1 – Unadjusted	0.54	0.48, 0.61
Model 2 – Risk-Adjusted	0.50	0.44, 0.56
Model 3 – Propensity-score adjusted	0.53	0.46, 0.59
Model 4 – Propensity-score matched	0.58	0.52, 0.63
Period 2 (2008-2014):		
Model 1 – Unadjusted	0.56	0.52, 0.61
Model 2 – Risk-Adjusted	0.54	0.49, 0.58
Model 3 – Propensity-score adjusted	0.54	0.49, 0.59
Model 4 – Propensity-score matched	0.58	0.52, 0.63

* *Note 1:* No significant interaction by sex or time period in unadjusted, risk-adjusted or propensity-score adjusted models.

† *Note 2:* Risk-adjusted models include age group, Charlson comorbidity index and admission status as covariates. Propensity score adjustment or matching was based on a logistic regression model that includes age group, Charlson comorbidity index and admission status as covariates.

Abbreviations: CI=Confidence Interval, IVIG=Intravenous Immunoglobulin, TPE = Therapeutic plasma exchange.

Table 4.

Linear regression models for treatment type as a predictor of $\log_e$-transformed total hospitalization charges – 2002-2014 Nationwide Inpatient Sample [*]

TPE vs. IVIG: [†]	**β**	**95% CI**
OVERALL:		
Model 1 – Unadjusted	0.20	0.16, 0.25
Model 2 – Risk-Adjusted	0.21	0.16, 0.26
Model 3 – Propensity-score adjusted	0.19	0.14, 0.24
Model 4 – Propensity-score matched	0.21	0.14, 0.29
MALE:		
Model 1 – Unadjusted	0.21	0.14, 0.27
Model 2 – Risk-Adjusted	0.19	0.13, 0.25
Model 3 – Propensity-score adjusted	0.19	0.12, 0.25
Model 4 – Propensity-score matched	0.22	0.13, 0.31
FEMALE:		
Model 1 – Unadjusted	0.20	0.13, 0.27
Model 2 – Risk-Adjusted	0.24	0.17, 0.30
Model 3 – Propensity-score adjusted	0.19	0.11, 0.26
Model 4 – Propensity-score matched	0.19	0.09, 0.29
Period 1 (2002-2007):		
Model 1 – Unadjusted	0.39	0.32, 0.47
Model 2 – Risk-Adjusted	0.31	0.23, 0.38
Model 3 – Propensity-score adjusted	0.38	0.31, .46
Model 4 – Propensity-score matched	0.39	0.31, 0.49
Period 2 (2008-2014):		
Model 1 – Unadjusted	0.32	0.26, 0.37
Model 2 – Risk-Adjusted	0.31	0.25, .36
Model 3 – Propensity-score adjusted	0.30	0.24, .36
Model 4 – Propensity-score matched	0.33	0.25, 0.40

[*] *Note 1:* No significant interaction by sex or time period in unadjusted, risk-adjusted or propensity-score adjusted models.

[†] *Note 2:* Risk-adjusted models include age group, Charlson comorbidity index and admission status as covariates. Propensity score adjustment or matching was based on a logistic regression model that includes age group, Charlson comorbidity index and admission status as covariates.

Abbreviations: CI=Confidence Interval, IVIG=Intravenous Immunoglobulin, TPE = Therapeutic plasma exchange.

Table 5.

Logistic regression models for treatment type as a predictor of in-hospital death – 2002-2014 Nationwide Inpatient Sample [*]

TPE vs. IVIG: [†]	**OR**	**95% CI**
OVERALL:		
Model 1 – Unadjusted	2.78	1.99, 3.88
Model 2 – Risk-Adjusted	2.57	1.82, 3.62
Model 3 – Propensity-score adjusted	2.48	1.77, 3.48
Model 4 – Propensity-score matched	2.91	2.03, 4.16
MALE:		
Model 1 – Unadjusted	2.62	1.68, 4.08
Model 2 – Risk-Adjusted	2.34	1.49, 3.66
Model 3 – Propensity-score adjusted	2.33	1.49, 3.64
Model 4 – Propensity-score matched	2.84	1.76, 4.59
FEMALE:		
Model 1 – Unadjusted	3.02	1.82, 5.00
Model 2 – Risk-Adjusted	2.98	1.76, 5.07
Model 3 – Propensity-score adjusted	2.71	1.62, 4.53
Model 4 – Propensity-score matched	2.99	1.69, 5.26
Period 1 (2002-2007):		
Model 1 – Unadjusted	3.44	1.83, 6.44
Model 2 – Risk-Adjusted	3.08	1.60, 5.94
Model 3 – Propensity-score adjusted	3.07	1.64, 5.79
Model 4 – Propensity-score matched	3.39	1.77, 6.48
Period 2 (2008-2014):		
Model 1 – Unadjusted	2.58	1.72, 3.89
Model 2 – Risk-Adjusted	2.29	1.51, 3.47
Model 3 – Propensity-score adjusted	2.29	1.51, 3.48
Model 4 – Propensity-score matched	2.80	1.77, 4.45

[*] *Note 1:* No significant interaction by sex or time period in unadjusted, risk-adjusted or propensity-score adjusted models.

[†] *Note 2:* Risk-adjusted models include age group, Charlson comorbidity index and admission status as covariates. Propensity score adjustment or matching was based on a logistic regression model that includes age group, Charlson comorbidity index and admission status as covariates.

Abbreviations: CI=Confidence Interval, IVIG=Intravenous Immunoglobulin, OR=Odds Ratio, TPE = Therapeutic plasma exchange.