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Time to Invasive Airway Placement and Resuscitation Outcomes After Inhospital Cardiopulmonary Arrest

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For the American Heart Association National Registry of Cardiopulmonary Resuscitation Investigators.

Abstract

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Background—Clinicians often place high priority on invasive airway placement during cardiopulmonary resuscitation. The benefit of early versus later invasive airway placement remains unknown. In this study we examined the association between time to invasive airway (TTIA) placement and patient outcomes after in-hospital cardiopulmonary arrest (CPA).

Methods—We analyzed data from the National Registry of Cardiopulmonary Resuscitation (NRCPR). We included hospitalized adult patients receiving attempted invasive airway placement (endotracheal intubation, laryngeal mask airway, tracheostomy, and cricothyrotomy) after the onset of CPA. We excluded cases in which airway insertion was attempted after return of spontaneous circulation (ROSC). We defined TTIA as the elapsed time from CPA recognition to accomplishment of an invasive airway. The primary outcomes were ROSC, 24-hour survival, and survival to hospital discharge. We used multivariable logistic regression to evaluate the association between the patient outcome and early (<5 minutes) versus later (≥5 minutes) TTIA, adjusted for hospital location, patient age and gender, first documented pulseless ECG rhythm, precipitating etiology and witnessed arrest.

Results—Of 82,649 CPA events, we studied the 25,006 cases in which TTIA was recorded and the inclusion criteria were met. Observations were most commonly excluded for not having an invasive airway emergently placed during resuscitation. The mean time to invasive airway placement was 5.9 minutes (95% CI: 5.8 - 6.0). Patient outcomes were: ROSC 50.3% (49.7% - 51.0%), 24-hour survival 33.7% (33.1% - 34.3%), survival to discharge 15.3% (14.9% - 15.8%). Early TTIA was not associated with ROSC (adjusted OR: 0.96, 0.91 - 1.01) but was associated with better odds of 24-hour survival (adjusted OR: 0.94, 0.89 - 0.99). The relationships between TTIA and survival to discharge could not be determined.

Conclusions—Early invasive airway insertion was not associated with ROSC but was associated with slightly improved 24-hour survival. Early invasive airway management may or may not improve in-hospital cardiopulmonary resuscitation outcomes.

INTRODUCTION

Despite ongoing efforts to improve quality of resuscitation care, survival after cardiopulmonary arrest (CPA) remains poor, with fewer than 17% of in-hospital arrest and only 8% of out-of-hospital arrest patients surviving to hospital discharge.¹⁻³ In both in-hospital and out-of-hospital settings, practitioners often emphasize early invasive airway placement or endotracheal intubation. The current literature, however, highlights the importance of other concurrent resuscitation actions such as continuous chest compressions and prompt vasoactive drug delivery.⁴ Most recently, Bobrow, et al. noted a significant increase in out-of-hospital cardiac arrest survival using a strategy of minimally interrupted CPR accompanied by delayed endotracheal intubation.⁵ The relative benefit of early versus later invasive airway placement remains undefined. A better understanding of this relationship could help to identify the optimal sequence of interventions for resuscitating patients in CPA.

In this study we examined the association between time to invasive airway (TTIA) and outcomes after in-hospital CPA.

METHODS

The University of Pittsburgh Institutional Review Board approved this study.

We used data from the American Heart Association's National Registry of Cardiopulmonary Resuscitation (NRCPR). Initiated in 2000, the NRCPR is an ongoing, international, multicenter registry of cardiopulmonary arrests (CPA) occurring at facilities in the United States, Canada, and Germany. The registry represents the largest collection of international

in-hospital CPA events ever compiled, and has provided the basis for several studies of CPA.^{1, 6-8} At the time of this study, the NRCPR contained data on over 120,000 CPA from more than 430 hospitals.

The NRCPR defines CPA as either pulselessness or inadequate perfusion requiring chest compressions or defibrillation, eliciting either a hospital-wide or unit-based emergency response by acute care facility personnel. The beginning of an event is defined as the time the need for chest compressions or defibrillation is first identified. The end of an event occurs when sustained return of spontaneous circulation is achieved for at least 20 minutes without need for further chest compression or when efforts are terminated and the patient is declared dead. Patients with known Do Not Resuscitate (DNR) orders and patients meeting brain death criteria are not included in the registry.

For this analysis we included adults ≥ 18 years experiencing CPA and receiving invasive airway management efforts. We defined invasive airway management as endotracheal intubation, laryngeal mask airway placement, tracheostomy or cricothyroidotomy. We included only patients receiving an invasive airway after CPA onset but before ROSC. We included cases from the study period January 1, 2003 to December 31, 2007.

We excluded patients with an invasive airway present prior to CPA onset, and those that received an invasive airway more than 60 minutes after the beginning of resuscitation. We excluded patients who did not require ventilation and those who were not ventilated, because they did not stand to potentially gain from ventilation through an invasive airway device. If the patient experienced more than one CPA during their admission, we included only the index event in the analysis. We excluded patient weight outliers (more than 250kg or less than 20kg) because such patients likely received extraordinary non-standard airway management. Patients were also excluded if the record indicated that they had advance directives that restricted resuscitation efforts.

The key variable of interest was time to invasive airway (TTIA), defined as elapsed time from recognition of CPA to the time of invasive airway placement, as indicated by NRCPR data. We excluded cases where TTIA was unknown or invalid. Based upon a preliminary examination of the unadjusted data, we observed that ROSC declined from 50.7% in the first minute to 49.2% after the tenth minute, crossing 50% in the seventh minute. In addition, the NRCPR's Scientific Advisory Board and the Emergency Cardiac Care Committee of the American Heart Association have recommended that invasive airway placement should occur within 5 minutes, and that time to invasive airway should be considered a "Process Gold Standard" for resuscitation.^{9, 10} For those reasons we dichotomized TTIA at 5 minutes ("1" = ≥ 5 minutes, "0" = < 5 minutes), characterizing "late" versus "early" time to invasive airway.

The key outcomes were return of spontaneous circulation (ROSC), 24-hour survival, and survival to hospital discharge.

We evaluated the associations between each outcome and TTIA using multivariate logistic regression. We adjusted the models for hospital CPA location (inpatient floor, intensive care unit, step down unit, emergency department, or other), patient age ≥ 70 years old, female sex, first documented ECG rhythm (ventricular fibrillation and tachycardia vs. other rhythms), precipitating etiology (non-cardiac medical condition, cardiac medical condition, non-cardiac surgical condition, cardiac surgical condition, and other), and whether the CPA was witnessed. We verified model fit using the Hosmer-Lemeshow goodness of fit test.

Because respiratory distress may influence TTIA, we repeated the analysis separately for patients whose cause of CPA was acute respiratory insufficiency. To account for other

potential functional forms for TTIA, we repeated the analysis characterizing TTIA as ordinal and continuous variables. We also considered a piecewise splined regression with knots at every minute for the first ten minutes, an approach conceptualizing a different outcome-TTIA relationship for each 1-minute interval. We also fit multivariate fractional polynomial models to identify other potential relationships. We performed all analyses using Stata 9.2 (College Station, TX).

RESULTS

Of the 82,649 events in the dataset we analyzed 25,006 cases meeting study inclusion criteria. Observations were most commonly excluded for not having an invasive airway emergently placed during the resuscitation ($n=40,772$). The mean time to invasive airway was 5.9 minutes (95% CI: 5.8, 6.0). Early airway placement occurred in 10,956 events (43.8%), and later placement occurred in 14,050 (56.2%). (Table 1)

ROSC occurred in 12,590 events (50.3%; 95% CI 49.7%, 51.0%), and 8,413 patients (33.7%; 33.1-34.3%) of those survived for 24 hours. Only 3,828 CPA patients survived to hospital discharge (15.3%; 14.9-15.8%). Of the 3,824 hospital survivors with a recorded CPC score, 2,777 (72.6%; 71.2-74.0%) had favorable neurological outcome of cerebral performance category (CPC) of 1 or 2 at discharge or had no deterioration in CPC from admission to discharge. (Table 1)

Compared with later TTIA, early TTIA was not associated with ROSC. (Table 2) Early TTIA was associated with slightly improved odds 24-hour survival. (Table 2) The model evaluating TTIA associations with survival to discharge demonstrated poor model fit, precluding formal inferences. Given the poor model fit for survival to discharge, a model examining the conditional outcome of discharge with favorable neurological outcome was not prudent. (Appendix 1, For Peer Review Only) Subgroup analysis of patients with CPA precipitated by acute respiratory insufficiency showed no associations between early TTIA and ROSC or 24-hour survival. (Table 2) When repeating the analysis characterizing TTIA as continuous and ordinal variables, we observed no association with ROSC or 24-hour survival. (Appendix 2, For Peer Review Only). We similarly observed no associations with ROSC or 24-hour survival using fractional polynomial models. (Appendix 2, For Peer Review Only)

DISCUSSION

While invasive airway placement is given a high priority in cardiopulmonary resuscitation, our analysis suggests that early compared to later invasive airway placement does not improve odds of ROSC. This observation supports the notion that clinicians may delay -- or even defer -- invasive airway placement during the initial phases of cardiopulmonary resuscitation without adversely affecting ROSC. While early invasive airway placement is associated with slightly better odds of 24 hour survival, the effect size of early intervention is small, and differences in post-resuscitation care likely confound this result.

One possible explanation for the observed results is that invasive airway placement provides no additional benefit compared to bag-valve-mask ventilation alone during the initial phase cardiopulmonary resuscitation. This notion is consistent with the observation that the subgroup of patients whose CPA was precipitated by acute respiratory insufficiency did not benefit more from early TTIA than the rest of the study population. The goal of invasive airway management is to improve access to the lungs for respiratory gas exchange. In fact, there are very few direct comparisons of invasive airway management with bag-valve-mask ventilation in CPA patients.

Another plausible explanation for our finding is that early invasive airway placement interferes with accomplishment of other concurrent CPR interventions, offsetting any potential benefits. For example, invasive airway placement may impede CPR chest compressions. Coronary perfusion pressure is an important element for defibrillation success, and current Emergency Cardiac Care guidelines emphasize the key role of high-quality uninterrupted closed chest compressions. In an out-of-hospital CPA series, we found that endotracheal intubation caused over 90 seconds of CPR interruption.¹¹ Aufderheide, et al. identified post-intubation hyperventilation leading to compromised CPR coronary perfusion in out-of-hospital CPA patients.¹² Deferring invasive airway management may allow for fewer chest compression interruptions, more effective artificial circulation and greater defibrillation success.

Airway insertion efforts may also impede the delivery of resuscitation medications. Vasoactive drugs may augment coronary perfusion pressure and rescue shock outcome in prolonged ventricular fibrillation. Animal studies point to improved outcomes when resuscitation drugs are delivered promptly during prolonged cardiac arrest.⁴

Our findings contrast with Shy, et al. who found improved survival associated with early invasive airway placement.¹³ However, the Shy study examined 693 of 10,254 total out-of-hospital CPA at a single site (King County, WA). Time to intubation analysis excluded 93.2% of the total arrests. The analysis compared patients receiving intubation before or after 12 minutes of pulselessness. At 6-12 minutes of CPA, the “metabolic” stages of CPA may exhibit greater responsiveness to invasive airway placement.¹⁴ Our in-hospital series included 25,006 patients. By dichotomizing at 5 minutes, we may have analytically obscured this benefit. We did reanalyze the results using continuous and ordinal schemes for TTIA but similarly found no associations with ROSC.

In this study we could not verify an association between TTIA and survival to discharge or discharge neurological outcome. While this observation may be due to our selected approach, the lack of association may also signal the absence of a biological relationship with later downstream outcomes. Prior studies highlight the role of quality post-ROSC care on long term survival.¹⁵⁻¹⁷ In an out-of-hospital series we showed that patient characteristics and resuscitation processes of care posed different effects on early vs. late CPA survival.¹⁸ While we may have improved model fit with an alternate selection of covariates, we chose to retain the *a priori* defined covariates because they had strong clinical relevance. The use of different risk adjustment measures between models would have complicated the interpretation of the observed results.

This study has important limitations. The NRCPR is primarily a quality improvement tool and may be subject to reporting bias. The data may also be subject to recall bias. Intervention times, including TTIA, likely represented approximations of the actual treatment delivery times.

The data had only limited information regarding the course of airway management. For example, we were unable to determine the number of airway insertion attempts. Also, since individual sites reported these parameters inconsistently, we did not have access to adequate information regarding the quality of airway management; for example, multiple laryngoscopies or unrecognized esophageal intubation.

Our regression models may have failed to account for relevant factors or for confounders that were not measured or reported; for example, fatal adverse events unrelated to the airway management and differences in post-resuscitation care. Additionally, during our study period resuscitation guidelines were changed to emphasize chest compressions, and progress was made in therapeutic hypothermia and post-resuscitation care.⁴ Such secular shift may

have introduced some unaccounted heterogeneity into the data. Our inability to characterize the relationships between TTIA and hospital discharge potentially signals the presence of unaccounted confounders. Residual confounding should also be considered when interpreting the relationship between TTIA and 24-hour survival, especially since the observed effect of early invasive airway placement is small. Despite the limitations, our selected analytic approach represented the best strategy given the available data.

CONCLUSION

In this study, early invasive airway insertion was not associated with ROSC but was associated with slightly improved 24-hour survival. Early invasive airway management may not improve inhospital cardiopulmonary resuscitation outcomes.

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Appendix 1 (for peer review only)

(for peer review only). Odds ratios from multivariate logistic models predicting resuscitation outcomes from later rather than earlier time to invasive airway (TTIA). Models predicting survival to discharge had poor model fit by Hosmer-Lemeshow Goodness of Fit Test.

	ROSC OR (95% CI)	24-hour Survival OR (95% CI)	Survival to Discharge OR (95% CI)
Time to Invasive Airway			
TTIA ≥5 vs <5 minutes	0.96 (0.91-1.01) p = 0.11	0.94 (0.89-0.99) p=0.028	0.93 (0.86-1.00) p=0.038
Location			
Inpatient (referent)	-	-	-
ICU	1.5 (1.4-1.6)	1.2 (1.1-1.3)	1.3 (1.2-1.5)
Step Down	1.5 (1.4-1.6)	1.5 (1.4-1.7)	1.6 (1.5-1.8)
ED	2.3 (2.0-2.5)	2.0 (1.8-2.3)	2.7 (2.4-3.1)
OR + Other	1.6 (1.4-1.8)	1.8 (1.6-2.0)	2.1 (1.8-2.5)
Age			
≥70 vs. <70 years	0.9 (0.8-0.9)	0.8 (0.7-0.8)	0.7 (0.7-0.8)
Sex (Female vs. Male)	1.3 (1.2-1.4)	1.1 (1.0-1.2)	1.1 (1.1-1.2)
Initial Rhythm			
VT/VF vs. PEA/Asystole	1.4 (1.3-1.5)	1.7 (1.6-1.8)	2.5 (2.3-2.7)
Etiology			
Medical-NonCardiac (referent)	-	-	-
Medical-Cardiac	0.9 (0.8-0.9)	1.0 (0.9-1.0)	1.3 (1.2-1.4)
Surgical-NonCardiac	1.2 (1.1-1.2)	1.3 (1.2-1.4)	1.6 (1.4-1.8)
Surgical-Cardiac	1.4 (1.2-1.5)	1.8 (1.6-2.0)	2.6 (2.2-3.0)

	ROSC OR (95% CI)	24-hour Survival OR (95% CI)	Survival to Discharge OR (95% CI)
Other	1.4 (1.1-1.8)	1.7 (1.3-2.2)	2.5 (1.8-3.3)
Witnessed Arrest	1.4 (1.3-1.5)	1.3 (1.2-1.3)	1.6 (1.5-1.8)
Observations	24,993	24,967	24,980
Hosmer-Lemeshow Test	p=0.73	p=0.45	p=0.001

Appendix 2

Comparison of multivariable outcome models. Analyses of return of spontaneous circulation (ROSC) with time to invasive airway (TTIA) as a continuous variable in a logistic regression, as TTIA as an ordinal variable in a logistic regression, and TTIA as an ordinal variable in a multivariate fractional polynomial (MFP) logistic regression.

	ROSC TTIA as Continuous Variable Logistic Regression OR (95% CI)	ROSC TTIA as Ordinal Variable Logistic Regression OR (95% CI)	ROSC TTIA as Ordinal Variable MFP Logistic Regression OR (95% CI)
Time to Invasive Airway			
Continuous TTIA	1.00 (0.99-1.00) p=0.86	-	-
0-1 minute	-	ref.	ref.
1-2 minute	-	1.2 (1.0-1.3)	1.2 (1.0-1.3)
2-3 minute	-	1.1 (1.0-1.3)	1.1 (1.0-1.3)
3-4 minute	-	1.2 (1.0-1.3)	1.2 (1.0-1.3)
4-5 minute	-	1.1 (1.0-1.3)	1.1 (1.0-1.3)
5-6 minute	-	1.2 (1.0-1.3)	1.2 (1.0-1.3)
6-7 minute	-	1.1 (1.0-1.2)	1.1 (1.0-1.2)
7-8 minute	-	1.0 (0.9-1.2)	1.0 (0.9-1.2)
8-9 minute	-	1.1 (0.9-1.2)	1.1 (0.9-1.2)
9-10 minute	-	1.0 (0.8-1.1)	1.0 (0.8-1.1)
>10 minute	-	1.1 (0.9-1.2)	1.1 (0.9-1.2)
Location			
Inpatient (referent)	-	-	-
ICU	1.5 (1.4-1.6)	1.5 (1.4-1.6)	1.5 (1.4-1.6)
Step Down	1.5 (1.4-1.6)	1.5 (1.4-1.6)	1.5 (1.4-1.6)
ED	2.2 (2.0-2.5)	2.3 (2.0-2.5)	2.3 (2.0-2.5)
OR + Other	1.6 (1.4-1.8)	1.6 (1.4-1.8)	1.6 (1.4-1.8)
Age			
≥ 70 vs. <70 years	0.9 (0.8-0.9)	0.9 (0.8-0.9)	0.9 (0.8-0.9)
Sex (Female vs. Male)	1.3 (1.2-1.4)	1.3 (1.2-1.4)	1.3 (1.2-1.4)
Initial Rhythm			
VT/VF vs. PEA/Asystole	1.4 (1.3-1.5)	1.4 (1.3-1.5)	1.4 (1.3-1.5)
Etiology			

	ROSC TTIA as Continuous Variable Logistic Regression OR (95% CI)	ROSC TTIA as Ordinal Variable Logistic Regression OR (95% CI)	ROSC TTIA as Ordinal Variable MFP Logistic Regression OR (95% CI)
Medical-NonCardiac (referent)	-	-	-
Medical-Cardiac	0.9 (0.8-0.9)	0.9 (0.8-0.9)	0.9 (0.8-0.9)
Surgical-NonCardiac	1.1 (1.1-1.2)	1.1 (1.1-1.2)	1.1 (1.1-1.2)
Surgical-Cardiac	1.4 (1.2-1.5)	1.4 (1.2-1.5)	1.4 (1.2-1.5)
Other	1.4 (1.1-1.8)	1.4 (1.1-1.8)	1.4 (1.1-1.8)
Witnessed Arrest	1.4 (1.3-1.5)	1.4 (1.3-1.5)	1.4 (1.3-1.5)
Observations	24,993	24,993	24,993
Hosmer-Lemeshow Test		p=0.6024	p=0.6024

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Table 1

Study population characteristics.

	Total	TTIA < 5 minutes	TTIA ≥5 minutes
Observations	25,006	10,956 (43.8%)	14,050 (56.2%)
Time to Invasive Airway (Mean, IQR)	5.9 min, 2-8 min	2.1 min, 1-3 min	8.9 min, 5-10 min
Outcomes			
ROSC	12,590 (50.3%)	5,662 (51.7%)	6,928 (49.3%)
24 Hour Survival	8,413 (33.7%)	3,816 (34.9%)	4,597 (32.8%)
Survived to Discharge	3,828 (15.3%)	1,770 (16.16%)	2,058 (14.7%)
Favorable Neurological Discharge	2,853 (73.2%)	1,323 (73.5%)	1,530 (72.9%)
≥70 years old	13,213 (52.8%)	5,871 (53.6%)	7,342 (52.3%)
Location			
Inpatient	7,469 (29.9%)	2,982 (27.2%)	4,487 (31.9%)
ICU	7,603 (30.4%)	3,480 (31.8%)	4,123 (29.3%)
Step Down Unit	6,546 (26.2%)	2,709 (24.7%)	3,837 (27.3%)
ED	1,739 (7.0%)	985 (9.0%)	754 (5.4%)
OR & Other	1,649 (6.6%)	800 (7.3%)	849 (6.0%)
Female	10,433 (41.7%)	4,633 (42.3%)	5,800 (41.3%)
Initial Pulseless Rhythm VT or VF	4,226 (16.9%)	1,749 (16.0%)	2,477 (17.6%)
Etiology			
Medical - Not Cardiac	11,712 (46.9%)	5,120 (46.7%)	6,592 (47.0%)
Medical - Cardiac	8,765 (35.1%)	3,791 (34.6%)	4,974 (35.4%)
Surgical - Not Cardiac	2,937 (11.8%)	1,336 (12.2%)	1,601 (11.4%)
Surgical - Cardiac	1,323 (5.3%)	596 (5.4%)	727 (5.2%)
Other	260 (1.0%)	113 (1.0%)	147 (1.0%)
Witnessed Arrest	18,106 (72.4%)	8,359 (76.3%)	9,747 (69.4%)

Table 2

Odds ratios from multivariate logistic regression predicting return of spontaneous circulation (ROSC) and 24 hour survival from early (<5 minute) versus later (≥5 minute) time to invasive airway placement (TTIA), including those due to acute respiratory insufficiency..

	All Cases		Acute Respiratory Insufficiency Group Only	
	ROSC Multivariate Model OR (95% CI)	24-hour Survival Multivariate Model OR (95% CI)	ROSC Multivariate Model OR (95% CI)	24-hour Survival Multivariate Model OR (95% CI)
Time to Invasive Airway				
TTIA ≥ 5 vs. < 5 minutes	0.96 (0.91-1.01) p = 0.11	0.94 (0.89-0.99) p=0.028	0.99 (0.92-1.06) p=0.74	0.93 (0.86-1.01) p=0.089
Location				
Inpatient (referent)	-	-	-	-
ICU	1.5 (1.4-1.6)	1.2 (1.1-1.3)	1.5 (1.3-1.6)	1.3 (1.1-1.4)
Step Down	1.5 (1.4-1.6)	1.5 (1.4-1.7)	1.5 (1.3-1.7)	1.5 (1.4-1.7)
ED	2.3 (2.0-2.5)	2.0 (1.8-2.3)	2.1 (1.8-2.5)	1.9 (1.6-2.3)
OR + Other	1.6 (1.4-1.8)	1.8 (1.6-2.0)	1.6 (1.3-1.9)	1.9 (1.6-2.3)
Age				
≥ 70 vs. <70 years	0.9 (0.8-0.9)	0.8 (0.7-0.8)	0.9 (0.9-1.0)	0.8 (0.8-0.9)
Sex (Female vs. Male)	1.3 (1.2-1.4)	1.1 (1.0-1.2)	1.3 (1.2-1.4)	1.1 (1.0-1.2)
Initial Rhythm				
VT/VF vs. PEA/Asystole	1.4 (1.3-1.5)	1.7 (1.6-1.8)	1.1 (1.0-1.2)	1.3 (1.1-1.5)
Etiology				
Medical-NonCardiac (referent)	-	-	-	-
Medical-Cardiac	0.9 (0.8-0.9)	1.0 (0.9-1.0)	0.9 (0.9-1.0)	1.0 (0.9-1.1)
Surgical-NonCardiac	1.2 (1.1-1.2)	1.3 (1.2-1.4)	1.2 (1.1-1.4)	1.4 (1.2-1.5)
Surgical-Cardiac	1.4 (1.2-1.5)	1.8 (1.6-2.0)	1.3 (1.1-1.6)	1.7 (1.4-2.0)
Other	1.4 (1.1-1.8)	1.7 (1.3-2.2)	1.3 (0.9-1.9)	1.5 (1.1-2.2)
Witnessed Arrest	1.4 (1.3-1.5)	1.3 (1.2-1.3)	1.2 (1.1-1.3)	1.1 (1.0-1.2)
Observations	24,993	24,967	11,389	11,374
Hosmer-Lemeshow Test	p=0.73	p=0.45	p=0.81	p=0.41